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SURGICAL TREATMENT OF ACHALASIA OF THE ESOPHAGUS

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ALTHOUGH its etiology remains obscure, an experience of ten years' surgical treatment of achalasia of the esophagus has brought about a better understanding of the nature of the disease as it exists among patients who do not respond favorably to more conservative measures. It has become apparent that two distinct types can be differentiated on the basis of the clinical history, the x-ray examination and the anatomic appearance at operation.

TYPE 1 ACHALASIA

The more frequent type, comprising about 75 per cent of the cases, is that characterized by an enormous dilatation of the esophagus above the distal segment. The esophagus often assumes a sigmoid tortuosity and may accommodate large quantities of food and liquids. Patients with this form of the disorder do not experience pain, although the degree of dysphagia is often so severe that they become emaciated from inanition. At x-ray examination under the fluoroscope the greatly dilated esophagus is readily demonstrable, but there is a singular lack of peristaltic activity (Fig. 1). The terminal few centimeters of the esophagus may be identified by the occasional passage of a mere trickle of barium through into the stomach. When exposed at operation the terminal segment just proximal to the cardia is amazingly small in diameter, with abnormally thin muscular layers making a striking contrast with the enormously dilated, thick-walled portion above.

TYPE 2 ACHALASIA

Approximately 25 per cent of the cases present an entirely different picture. Patients with this type, at least early in the course of the disease, experience a certain degree of pain resulting from esophagospasm. This is referred to the substernal area, with radiation to the back at a slightly higher level. X-ray examination discloses a moderately dilated esophagus, which, however, never assumes the enormous proportions of the first type (Fig. 2). Fluoroscopic examination in this group reveals the presence of hyperactive esophageal peristalsis, which is, however, usually erratic and sometimes characterized by the occurrence of waves of contraction that pass in an antiperistaltic direction. At operation the lower segment of the esophagus, unlike that of the first group, in which it appears atrophic, is actually thickened though not dilated as it is above this level. This appearance is due to the occurrence of a singular degree of hypertrophy of the circular muscle fibers in this portion.

Cases of this type have been observed for many years without any evidence of change. In fact, there is no evidence that one type of the disorder can evolve from the other even though both are characterized by the absence of the ganglion cells of the myenteric plexus.

RATIONALE OF SURGICAL TREATMENT

It is generally accepted that conservative measures, including bougienage, should be given an adequate trial before surgery is resorted to. It is difficult to understand why one or two dilatations of the lower esophagus may be followed by long-lasting, complete relief of dysphagia in many patients whereas in others the benefit is slight and transitory. The fact remains, however, that in a small number of patients the response to dilatation is unsatisfactory and something further must be done. Some patients, also, object to treatment by bougienage and thereby become candidates for surgical relief.

The first 6 patients of this series were treated by resection of the lower segment of the esophagus followed by an esophagogastric anastomosis. Although complete relief from dysphagia is easily accomplished by this means, the operation was soon abandoned because it was obviously too radical and it was recognized that the same result could be accomplished by other measures. The next procedure employed was an esophagoplasty, previously described,[1] whereby a longitudinal incision was made through

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the entire length of the narrow lower segment followed by a circumferential closure of the opening. By this means the narrowed segment is eliminated, the lumen at the lower end assumes a large diameter, and the relief from dysphagia is complete and permanent. As more patients were observed, however, the existence of the type of case characterized by

FIGURE 1. *Roentgenogram after Ingestion of Barium by a Fifty-six-Year-Old-Man with Type 1 Achalasia of the Esophagus, Showing Tortuosity and Enormous Dilatation, with a Mere Trickle of Barium Passing through the Narrowed Distal Esophageal Segment.*

hypertrophy of the circular muscle fibers of the distal segment was recognized. For these cases, therefore, a modification of the Heller esophagomyotomy, consisting of a single lengthwise incision through the thickened circular muscle fibers of the lower segment, was adopted.

Although the results of esophagomyotomy employed only for the management of the cases with circular-muscle-fiber hypertrophy have been preeminently satisfactory in the small series of cases reported, a comparison with the experience of others who have used this procedure routinely in all cases indicates that relief is not obtained uniformly. This may be because the procedure is not so successful when the distal segment presents an atrophic, thinned-out muscle layer.

Since it was recognized that there are two distinct types of the disease from the anatomic point of view, it has been the policy in the management of the patients described below to employ an esophagoplasty (longitudinal incision and circumferential closure) for Type 1 lesions, in which there is a thin, atrophic muscle layer at the lower end, and an esophagomyotomy (modified Heller operation) in Type 2 disease, in which the distal segment is characterized by hypertrophy of the circular muscle fibers.

Because all the 48 patients treated are included in this series, it should be mentioned that in the beginning, when the open esophagoplasty was employed, the importance of maintaining the stomach in a normal position below the diaphragm was not realized. This probably accounts for the greater occurrence of regurgitation from the stomach into the esophagus in some of these patients. More recently, when this operation has been employed, great pains have been taken to maintain as normal as possible the anatomic relation of the cardia and lower esophagus with the esophageal hiatus of the diaphragm.

COMPOSITION OF SERIES

Achalasia of the esophagus may be observed in patients of all ages (Table 1). The youngest of the

FIGURE 2. *Roentgenogram of the Lower Portion of the Esophagus after Ingestion of Barium by a Forty-nine-Year-Old Man with Type 2 Achalasia of the Esophagus, Showing the Relatively Minor Degree of Dilatation of the Esophagus Characteristic of This Type.*

group was two years old; another was a child of eleven years. Three others were under the age of twenty. The remainder were spread out over all the decades of adult life up to old age. The oldest patient was seventy-four.

Sex

Although there were many more women than men in the entire series (29 as opposed to 19), it is inter-

esting that of the 10 patients treated by esophagomyotomy (Type 2 disease, with hypertrophy of circular muscle), 8 were men and only 2 were women. Whether or not Type 2 achalasia predominates in men is not known.

Duration of Symptoms

The duration of symptoms showed wide variations, from one or two years up to as long as forty years in 1 case. The majority of patients (32 in all) had experienced symptoms for less than eleven years. The details are given in Table 2.

Types of Operation and Operative Mortality

A resection was performed as the primary procedure in 6 patients (Table 3). Five of these were treated early in my experience, as mentioned above. The sixth required a resection because of a coexisting gastric ulcer. In 6 other patients a resection was performed because of the failure of a previous surgical procedure. Two patients (Group A) were treated first by esophagoplasty but had to have a radical proximal gastrectomy with esophagogastric anastomosis because of hemorrhage from severe gastritis. The other 4 (Group B) had been operated on first elsewhere by some form of esophagoplastic procedure or by a lateral anastomosis between the gastric fundus and the esophagus, and reoperation was carried out because of obstruction. There were no postoperative deaths among the 12 patients treated by either primary or secondary resection.

An esophagoplasty of the type already described was carried out in 28 patients. Two of these, as already mentioned, were subsequently reoperated on by resection, leaving 26 in whom an esophagoplasty was the only procedure performed. In this group there were 2 postoperative deaths. One of these occurred from a transfusion reaction resulting from the administration of mismatched blood. The other death was that of an elderly patient (seventy-four years of age) who was in poor condition because of inanition. Death (on the nineteenth day after operation) was caused by uncontrollable hemorrhage into the gastrointestinal tract from diffuse severe gastritis and esophagitis.

The remaining 10 patients of the series were treated by esophagomyotomy. None of these died after operation.

TABLE 1. *Age Distribution.*

AGE	NO. OF PATIENTS
yr.	
1-10	1
11-20	4
21-30	9
31-40	7
41-50	12
51-60	9
61-70	5
71-80	1
Total	48

TABLE 2. *Duration of Symptoms.*

DURATION	NO. OF CASES
yr.	
0-5	21
5-10	11
11-20	5
21-30	4
31-40	1
Indefinite	6
Total	48

Subsequent Deaths

Of the 46 patients who survived the operation and left the hospital in good condition 2 died at a later date. One, a thirty-nine-year-old woman who had been treated by primary resection, died a year later of cerebral thrombosis. The other, a fifty-one-year-old man who had been treated by esophagoplasty with excellent results, died fourteen months later of an

TABLE 3. *Analysis of Series.*

TYPE OF OPERATION	NO. OF CASES	OPERATIVE DEATHS	SUBSEQUENT DEATHS	NO FOLLOW-UP STUDY	OPERATION TOO RECENT FOR ANALYSIS	PATIENTS REPORTING FOR EXAMINATION	PATIENTS FOLLOWED BY MAIL
				NO. OF CASES	NO. OF CASES		
Primary resection	6	0	1	1	0	4	0
Secondary resection:							
Group A	2	0	0	0	0	2	0
Group B	4	0	0	1	0	3	0
Esophagoplasty	26	2	1	2	3	11	7
Esophagomyotomy	10	0	0	0	3	7	0
Totals	48	2	2	4	6	27	7

acute episode characterized by agonizing precordial pain thought by his physician to be due to a massive coronary occlusion.

Method of Follow-up Study

Accurate information for analysis of the results (Table 3) was obtained in 34 living patients—7 by mail, usually from their physicians, and 27 by personal interview, including x-ray examination. Adequate information was available regarding the condition of 2 others who died of unrelated causes long after the operation performed for relief of achalasia. In 6 the operation was thought to be too recent for significant data to be obtained.* It was impossible to reach the remaining patients.

TABLE 4. *Late Postoperative Symptoms.*

Symptom	Primary Resection	Secondary Resection	Esophagoplasty	Esophagomyotomy	Totals
	No. of cases	No. of cases	No. of cases	No. of cases	
Dysphagia:					
Permanent relief	3	5	13	6	27
Occasional spasm	1	0	5	1	7
Obvious stricture	0	0	2	0	2
Pyrosis:					
Slight	0	1	8	1	10
Moderate	0	0	1	0	1
Severe	2	1	1	0	4
Regurgitation	2	4	5	0	11
Dumping syndrome	0	3	0	0	3
Bleeding:					
From gastritis	1	0	4	0	5
From esophagitis & gastritis	0	0	1	0	1
From carcinoma of sigmoid	0	1	0	0	1
Cause unknown	0	0	2	0	2
No symptoms	1	1	5	6	13
Total patients followed	4	5	20	7	36

Results of Investigation

In the first place, it should be pointed out that 13 patients experienced no postoperative symptoms of any kind and remained completely relieved. It should be mentioned also that some of those who experienced symptoms had more than one complaint.

Late Postoperative Symptoms

Table 4 enumerates the significant late symptoms and discloses their frequency of occurrence in the various groups according to the type of operation performed.

Complete and permanent *relief from dysphagia* was obtained in 27 of the 36 patients followed. Occasional transitory delay in the passage of food was described by 7 patients. One of these, a young man of considerable emotional instability on whom an esophagomyotomy was performed, experienced slight difficulty for a time when disturbed emotionally but otherwise remained free from symptoms. At present he observes no dietary restrictions and now, four years after operation, is completely well. The follow-up study of this patient has been unusually complete because of the interest of his physician. Another is one of the first patients operated upon by primary resection. In 2 patients stenosis developed at the site of an esophagoplasty, responding in each to bougienage. One of these experienced the lodgment of a large mouthful of meat on one occasion but has been free from obstruction since a dilatation was performed after the bolus had been extracted.

As shown in Table 4, severe degrees of *pyrosis* have occurred in 4 patients, a moderate amount in 1, and slight degrees in 10. This symptom occurred no more frequently after one type of operation than after any other. The exact cause of this symptom of stimulation of the lower esophagus is not always clear. It does not in itself signify the presence of esophagitis. Reference to this phenomenon and its relation to esophagitis was made in a previous communication.[2]

Regurgitation of fluid into the pharynx was observed by 11 patients about equally divided between those who had had a resection and those who had had an esophagoplasty. Regurgitation has not been experienced by any of the patients who had an esophagomyotomy. It should be noted, however, that regurgitation into the lower esophagus is frequently observed at fluoroscopic examination even in normal persons and is not, therefore, significant unless severe in degree.

Three patients, all of whom had had a secondary resection, experienced the so-called *"dumping syndrome."* This observation is not particularly significant in this group, however, because such symptoms are frequently encountered among patients who have had a partial esophagectomy and proximal gastrectomy for any cause, whether carcinoma or benign lesions other than achalasia.

Bleeding apparently from the upper gastrointestinal tract was experienced by 9 patients. In 3 it was manifested merely by a moderate degree of chronic anemia resulting from slow oozing of blood from chronic gastritis demonstrated by esophagoscopic observation. In 2 the exact source was not demonstrated, but gastritis was suspected. All these responded to medical measures, and the blood loss eventually ceased.

In 1 other case, although gastritis or esophagitis

*Subsequent reports indicate that all are doing well.

was originally suspected, the source of chronic blood loss was found ultimately to have been a carcinoma of the sigmoid.

In 3 patients the bleeding was massive enough to endanger life. One of these, whose case was alluded to above, died nineteen days postoperatively of uncontrollable hemorrhage from acute gastritis and esophagitis as proved by subsequent post-mortem examination. In the other 2 patients, each of whom had been treated originally by esophagoplasty with an excellent mechanical result, the source of bleeding was found at operation to be acute gastritis. In 1 of these there was also esophagoscopic evidence of esophagitis, with an ulcer at the suture line. An extensive proximal partial gastrectomy, with re-anastomosis by end-to-end approximation of the small gastric remnant with the esophagus, was followed by permanent correction of the difficulty in both patients.

It should be emphasized that in 6 of the 9 patients who were known to have experienced bleeding from the gastrointestinal tract at some time after the operation performed for the relief of achalasia of the esophagus, the source of the hemorrhage was proved to be the hyperemic congestion of the gastric mucosa characteristic of gastritis. Proof of this fact rests on esophagoscopic observation alone in 3 patients, on the findings at operation alone in 1 patient, on both esophagoscopy and observation made at operation in 1 patient and on autopsy in another.

In 2 other cases, as mentioned above, the cause was not actually demonstrated although gastritis was suspected on the basis of x-ray studies.

Esophagitis was observed only in the patient on whom an autopsy was performed, but in the opinion of the pathologist the principal source of the bleeding in this case was the massive gastritis.

A fact of great importance in these cases, commented on below, is that 5 patients had demonstrable spasm of the antral segment of the stomach and pylorus that would account for a considerable degree of delay in the emptying time of the stomach. This, as suggested by the work of Dragstedt et al.,[3] may have been a contributing cause of the gastritis that was the source of the bleeding in all these patients. One of this group is of particular interest. He was treated originally by partial proximal gastrectomy and esophagectomy rather than by esophagoplasty because he had a gastric ulcer close to the cardia at the time of operation. His response to operation was unsatisfactory, however, both because he was unable to tolerate a sufficient volume of food to maintain adequate nutrition and because of chronic anemia shown later by esophagoscopy and at operation to be due to gastritis. The significance of the fact that he had a tight pylorus was not recognized at the time. Four years after the original operation a pyloroplasty was performed, with immediate and complete relief from both difficulties.

In 1 other patient a pyloroplasty was performed at the original operation, which was an esophagoplasty. She had a moderate anemia for a few weeks after the operation that responded well to the administration of iron. She has remained well ever since.

It should be stated that 2 of the 9 patients discussed above had evidence of previous ulcers in the duodenum. There was no indication, however, that the blood loss in either was caused by reactivation of the ulcer. Both had evidence of gastritis as the more probable source. It is not known whether chronic delay in gastric emptying, the result of a degree of partial obstruction from the ulcer scar, was a factor in the causation of the gastritis.

TABLE 5. *Results of Follow-up X-Ray Examination.*

FINDING	PRIMARY RESECTION	SECONDARY RESECTION	ESOPHAGOPLASTY	ESOPHAGOMYOTOMY	TOTALS
	NO. OF CASES	NO. OF CASES	NO. OF CASES	NO. OF CASES	
Total patients examined	4	5	13	7	29
Reduced diameter of esophagus	3	5	10	7	25
Regurgitation	0	0	0	0	0
Spasm of esophagus	0	0	2	1	3
Stricture	0	0	2	0	2
Ulcer of esophagus	0	0	0	0	0
Duodenal ulcer	1	0	1	0	2
Pyloric & antral delay	0	3	1	0	4

POSTOPERATIVE X-RAY FINDINGS

Table 5 lists the findings on routine examination of the 29 patients who were examined by fluoroscopy at the time of the follow-up study. It is interesting that the *diameter of the esophagus* was discovered to be obviously smaller than it was before operation in 25 patients of this group. One must not assume, however, that the esophagus ever becomes normal in these patients. The change noted is due merely to the fact that the influence of the obstructing lower segment has been overcome by the operation.

In no case was a significant degree of *regurgitation* from the stomach into the esophagus observed in spite of the fact that some of the patients reported that they felt as though regurgitation into the pharynx sometimes occurred. This may mean that the pharyngeal regurgitation observed clinically came actually from material lying in the esophagus and not from the stomach itself.

Occasional *esophagospasm* occurring during the ingestion of barium was seen in 1 of the patients who had a Heller operation. This patient, like 2 who had been treated by esophagoplasty, experienced no symptoms and was unaware of its occurrence.

As previously noted above, a moderate degree of *stenosis* was observed at the site of esophagoplasty in 1 patient.

No indication of *esophagitis* or *esophageal ulcer* was encountered in any of the 29 patients examined. On the other hand, evidence of a *duodenal ulcer* was seen in 2 patients previously mentioned.

Delay in the emptying of the stomach because of a disturbance of motility of the antrum and pylorus was observed in 4 patients. As mentioned above, severe gastritis requiring reoperation developed in 2 of these. In 1 of the others, a patient who had an esophagoplasty, no symptoms have resulted from this condition. In the fourth, a woman treated by secondary resection, food tolerance is somewhat limited, and she complains of pyrosis but is otherwise getting along very well.

TABLE 6. *Endoscopic Examination after Operation.*

TYPE OF OPERATION	PATIENT	INDICATION	FINDINGS				CORRECTIVE PROCEDURE
			STRICTURE	ULCER	ESOPHAGITIS	GASTRITIS	
Primary resection	M.S.T.	?Esophagitis	0	0	0	0	0
	S.R.	?Esophagitis	0	0	0	+	Pyloroplasty
Esophagoplasty	A.S.	Anemia	0	0	0	+	Resection
	G.R.	Dysphagia	0	0	+	–	Extraction of food
	M.S.	?Esophagitis	0	0	0	–	0
	G.M.	Dysphagia	0	0	+	+	Replacement of stomach
	D.L.	Anemia	0	+	+	–	Resection
Secondary resection	M.D.	Anemia	0	0	0	+	0

TABLE 7. *Weight at Follow-up Examination.*

OPERATION	NO. OF CASES	WEIGHT GAIN	NO CHANGE IN WEIGHT	WEIGHT LOSS	WEIGHT UNKNOWN
		NO. OF CASES	NO. OF CASES	NO. OF CASES	NO. OF CASES
Primary resection	4	2	1	1	—
Secondary resection	5	2	1	—	2
Esophagoplasty	20	9	—	4	7
Esophagomyotomy	7	7	—	0	—
Totals	36	20	2	5	9

POSTOPERATIVE ESOPHAGOSCOPIC EXAMINATION

Table 6 discloses the findings at esophagoscopy performed on 8 patients whose symptoms at one time or another after operation seemed to require it. The indications, findings and measures adopted to correct the difficulty are shown. In 3 cases the symptoms, including pyrosis and regurgitation, and in 1 a substernal feeling of fullness after eating gave rise to the suspicion that the patients might be suffering from esophagitis. Esophagitis, however, was not found in any of this group. In 2 the symptoms were unexplained. In the third, a patient already alluded to, a severe gastritis was disclosed, and complete relief followed the performance of a pyloroplasty.

In 3 patients the indication for esophagoscopy was the development of anemia, which was considered possibly due to esophagitis, as described by other authors. However, at esophagoscopy the bleeding was demonstrated in each case to be the result of gastritis, although 1 patient was found to have esophagitis as well, with an ulcer at the line of suture where an esophagoplasty had been performed. Two were treated by resection, as previously noted, and in the third a good response resulted from medical therapy and no further treatment was required.

Dysphagia (obstructive difficulty with swallowing) was the indication for examination in 2 patients who had been treated by esophagoplasty. One of these, a young woman operated on before the importance of leaving the stomach below the diaphragm at the completion of the esophagoplasty was recognized, was found to have both esophagitis and gastritis. A subsequent operation, at which the stomach was mobilized and the fundus and cardia replaced below the diaphragm, with a restoration of the esophageal hiatus to a normal diameter, resulted in relief of the difficulty.

WEIGHT

Table 7 shows the weight of the patients at follow-up examination as compared with that before the operation was performed. Twenty of the 27 whose preoperative weight had been recorded had experienced a gain of weight, sometimes amounting to 9.1 kg. (20 pounds) or 13.6 kg. (30 pounds), usually back to their normal level. In 2 cases there was no gain or loss, and in 5 there had been a loss. One of these resulted from dysphagia due to a stenosis at the site of esophagoplasty (already mentioned). Another patient, who was treated by pyloroplasty later, went from 81.6 kg. (180 pounds) to 61.7 kg. (136 pounds); after the pyloroplasty he had gained 5.4 kg. (12 pounds) while still in the hospital. In

2 of the others the loss was of no clinical significance — from 61.2 kg. (135 pounds) to 59.0 kg. (130 pounds) in 1 case and from 75.7 kg. (167 pounds) to 70.8 kg. (156 pounds) in the other. In the fifth patient, a young man who was actually too heavy at 74.0 kg. (163 pounds), a loss to 61.2 kg. (135 pounds) brought his weight to a more normal level.

Resumption of Occupation

As an important factor in the evaluation of the health of the group, the ability of each patient to carry on his usual work was determined. Table 8 shows the results. Twenty-nine of the 36 patients followed were able to carry on their usual work at full capacity, many for the first time in many years. Three were working at limited capacity: 1 had been treated by secondary resection because of hemorrhage from gastritis; another had experienced dysphagia from stenosis at the operative site after esophagoplasty; and the third was the woman in whom a carcinoma of the sigmoid requiring resection developed.

Table 8. *Resumption of Occupation.*

Operation	No. of Cases	Full Capacity	Limited Capacity	Patient Unable to Work	Capacity Unknown
		no. of cases	no. of cases	no. of cases	no. of cases
Primary resection	4	4	0	0	0
Secondary resection	5	3	2	0	0
Esophagoplasty	20	15	1	0	4
Esophagomyotomy	7	7	0	0	0
Totals	36	29	3	0	4

Table 9. *Evaluation of Result.*

Operation	Total No. of Cases	Cases in Group A*	Cases in Group B†	Cases in Group C‡	Cases in Group D§
Primary resection	4	3	1	0	0
Secondary resection	5	1	3	1	0
Esophagoplasty	20	8	5	3	4
Esophagomyotomy	7	7	—	—	—
Totals	36	19	9	4	4

*90-100% improvement.
†80-90% improvement.
‡70-80% improvement.
§ < 70% improvement.

Evaluation of End Result

Table 9 shows the results of an effort to evaluate the degree of improvement after operation in terms of percentage of normal, based on the patient's own estimate and the objective observation of two examiners, taking into account the findings of the x-ray examination and esophagoscopy when these procedures were employed. By means of these estimates, a degree of improvement was assigned in each case according to the following schedule: A, excellent result in all respects, estimated to be 90 to 100 per cent improvement (19 patients); B, improvement estimated to be 80 to 90 per cent of normal (these patients, 9 in number, are essentially well, holding responsible jobs and suffering only minor or occasional inconveniences, and all of them entirely satisfied with the result); C, improvement approximately 70 to 80 per cent of normal (2 of these 4 patients had not returned to full employment, 2 others were having symptoms but thought that the operation had been beneficial and stated that they would have it again if confronted with the same condition that they had before, and 1 believed that the operation had saved her life); and D, less than 70 per cent (4 patients already mentioned, 2 of whom bled so extensively from gastritis that a resection had to be performed and 2 of whom had stenosis at the site of an esophagoplasty, requiring bougienage for relief).

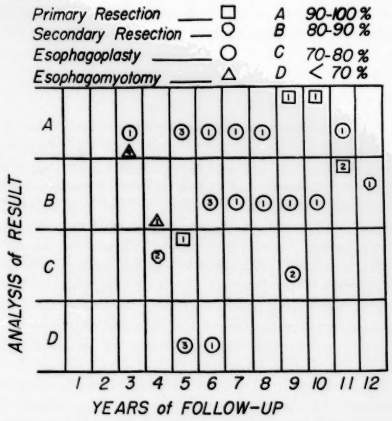

Figure 3. *Duration of Follow-up Study and Results Obtained, according to the Type of Operation Performed, in 34 Patients Operated on Three or More Years before the Study Was Made.*

Length of Follow-up Period

Figure 3 represents an effort to show in graphic form the duration of the follow-up period in terms of end results, according to the type of operation employed. Of the 34 patients followed for three or more years, 14 were classified as showing a 90 to 100 per cent degree of improvement (A result) and 11

as showing an 80 to 90 per cent degree of improvement (B result). Five patients whose result was classified as C were followed, 2 for four years, 1 for five years, and 2 for nine years. Those whose result was called D included 3 who were followed for five years and 1 followed for six years.

Further subdivision according to the type of operation performed is impracticable because of the small numbers of cases in each group, but of 21 treated by esophagoplasty and followed for three years or more, 8 had an A result, 7 a B result, 2 a C result, and 4 a D result (representing a complete failure to relieve symptoms). Of those treated by esophagomyotomy, 4 with an A result had been operated on three years, and 1 with a B result had been operated on four years previously.

Discussion

Types of Operation

The results of esophagomyotomy were entirely satisfactory. It should be recalled that this operation was chosen only in cases in which the lower segment of the esophagus was found to have a much hypertrophied circular muscle layer (Type 2 achalasia). All 4 of the poor results occurred in patients who had been treated by esophagoplasty. These have already been discussed. Recognition of the role of delayed emptying of the stomach in the development of gastritis might have made it possible to avoid the difficulties experienced by these patients. Three others of this group did not experience an outstandingly good result, but 13 of the 20 patients followed had an A or B result. Two have since died of intercurrent disease; 11 remain essentially well. The failure to realize the importance of restoring normal relations of the gastric cardia and the diaphragm at the esophageal hiatus in some of the earlier cases undoubtedly accounts for some of the disappointments in this group. As for the resection groups taken together, the ultimate results were good to excellent in the majority of cases, with no poor results and only 1 C result (70 to 80 per cent improvement).

Role of the Antrum and Pylorus

There is evidence that some patients with achalasia of the esophagus have some degree of coexisting disturbance of the motility of the stomach as well. This disturbance might be called pylorospasm. Jones[4] has pointed out, however, that although the pylorus participates in the occurrence of spasm of the lower end of the stomach, there is usually actually a more widespread spastic disturbance involving the antrum, the pylorus and often the first portion of the duodenum as well. This phenomenon may be observed under various circumstances, one of which is the condition mentioned here. This situation was recognized at operation in 1 patient, and a pyloroplasty was carried out as a part of the original procedure. Several other patients would have been better off, even to the extent of avoiding late complications, if this had been known. One of these, as already mentioned, was treated by pyloroplasty four years after his original operation. Furthermore, the postoperative development of delay in the emptying of the stomach caused by the disturbed motility of the antrum and pylorus that follows vagus-nerve section is a serious objection to the employment of resection in patients with achalasia.

The effect of delayed gastric emptying may be twofold. In the first place, it is obvious that when food does not leave the stomach readily, the patient's ability to eat is curtailed, and often his nutrition is impaired. Furthermore, the fact that the stomach may remain filled for hours after a meal and will not therefore accept more food for a prolonged period may lead the patient to believe that the obstruction of the lower esophagus has not been relieved. Likewise, delayed gastric emptying undoubtedly accounts for the symptoms of regurgitation or even of pyrosis experienced after the operation. The importance of this knowledge will be obvious to those who are familiar with the condition of patients who have been subjected to a proximal partial gastrectomy for any cause.

A second and most important effect of spasm at the distal end of the stomach, with its resultant delay in emptying of the stomach, has been elucidated by the recent work of Dragstedt et al.,[3] who have shown that even though the neurogenic factor in the production of acid gastric secretions is abolished by vagotomy, the hormonal stimulation produced by the secretion of the antral mucosa remains. They have demonstrated that the effect of hormonal stimulation of the antrum is greatly augmented by prolonged contact with food lying in the antral region for too long a period after its ingestion as a result of delay in the passage of material through the pylorus. This factor helps explain the otherwise little understood development of severe gastritis in some of these patients, 1 of whom actually had a gastric ulcer and pre-existing pylorospasm before he was originally operated on. Furthermore, the stasis resulting from hypomotility of the stomach and spasm at the inferior end undoubtedly contribute to the development of the hyperemic congestion of the gastric mucosa, a condition that favors the occurrence of bleeding from this membrane. It is suggested, therefore, that the frequency of gastritis after operations performed for the relief of dysphagia from achalasia in this group of patients, whether by resection or by esophagoplasty, is probably due to this mechanism.

Blood Loss after Operation

Frequent comment has been made that anemia from chronic blood loss or massive bleeding as an episodic occurrence is a common experience after open operations such as esophagoplasty or resection

done to relieve achalasia of the esophagus. Barrett and Franklin[5] and others have alluded to this point. The assumption has been made in most cases that the source of this bleeding is esophagitis induced, it is thought, by regurgitation of gastric secretions. In contrast to these opinions it is interesting that among the 8 patients in this series who had postoperative bleeding from the upper gastrointestinal tract, with the exception of 1 who bled obviously from esophagitis, the bleeding came only from the stomach and was proved to be the result of severe gastritis in 6 cases. The possible role of delayed gastric emptying in the development of this condition, as suggested by Dragstedt's work, has already been mentioned as the most likely explanation.

Summary and Conclusions

Two types of achalasia of the esophagus must be recognized.

When surgical relief of the condition becomes necessary, it seems reasonable to employ, in Type 1 cases, with a thin, atrophic muscle layer at the lower end, a simple esophagoplastic procedure consisting of a longitudinal incision through the narrowed atrophic lower segment followed by a circumferential closure of the opening. Suggestions are made, on the basis of experience with this series, for avoiding some of the complications observed in patients treated early in the development of this experience. For those who have Type 2 achalasia, with hypertrophy of the circular muscle fibers in the lower segment, esophagomyotomy by a modification of the Heller technic is pre-eminently satisfactory.

Delayed emptying of the stomach due to altered motility and spasm of the antrum and pylorus, which may be an accompaniment of the disease or which may develop after certain operations, notably resection involving interruption of both vagus nerves, must be overcome by pyloroplasty to avoid the untoward or actually hazardous effects of delayed gastric emptying. These are hemorrhage from gastritis, food intolerance and the train of symptoms resulting from regurgitation into the esophagus.

On the basis of the experience reported above, at least 80 per cent of the patients operated on for achalasia of the esophagus should have good to excellent results.

It is hoped that the results can be improved by observation of some of the principles learned by experience in the treatment of this group of patients and by a greater employment of esophagomyotomy in the management of suitable cases.

I am indebted to Dr. L.L. Robbins, chief of the Department of Roentgenology, Massachusetts General Hospital, who made the follow-up x-ray examinations, to Drs. F. Thomas Gephart and Dr. E.W. Wilkins, Jr., for the follow-up interviews of patients, and to Dr. Edward B. Benedict, who carried out the endoscopic examination in this series.

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APPLICATION OF THE ANTISTREPTOLYSIN-O TITER IN THE EVALUATION OF JOINT PAIN AND IN THE DIAGNOSIS OF RHEUMATIC FEVER*

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A RECENT review of the literature[1] and our own experience at the House of the Good Samaritan[2-5] suggest that early treatment of rheumatic fever with ACTH and cortisone may prevent or mitigate heart damage. Early treatment is dependent on early diagnosis of the disease. Clinically, rheumatic fever is diagnosed by such manifestations as subcutaneous nodules, chorea, erythema marginatum, carditis and arthritis. Subcutaneous nodules are a late manifestation, and chorea and erythema marginatum occur sometimes early but also frequently late in the course of the disease. When definite carditis (significant murmurs or congestive heart failure) has been established, some irreversible damage may have already occurred. Joint pain, in contrast to other signs and symptoms, is a frequent early manifestation, but it is regarded as unreliable because so many other diseases may produce this symptom.

The foregoing considerations led us to select a simple, technically reliable laboratory test that might help us to differentiate the joint pain of rheumatic fever from that of other diseases.

Most investigators now agree that rheumatic fever is precipitated by an antecedent infection with Group

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A streptococci and that consequently streptococcal antibodies, including the antistreptolysin-O titer, are generally found to be high in patients with active rheumatic fever.[6-9] Since we have been determining antistreptolysin-O titers routinely for our own patients as well as for patients from other hospitals and private physicians since 1939, it seemed worth while to review the data concerning antistreptolysin-O titers in those of our patients believed to have definite rheumatic fever, in patients with rheumatoid arthritis (Still's disease), and in patients with joint and extremity pain from a variety of other causes.

The main purpose of this paper is to present these data and to show the extent to which the antistreptolysin-O titer may be utilized in the differentiation of the joint pain of rheumatic fever from that of other diseases. It is also the purpose of this paper to consider the frequency and importance of joint pain as a manifestation of rheumatic fever.

Clinical Material

The clinical material utilized for this study consists of four groups of patients who were admitted to the House of the Good Samaritan or the Children's Hospital between January, 1940, and December, 1953.

Group 1

Group 1 comprises 208 consecutive patients with cardiac involvement below the age of seventeen years admitted to the House of the Good Samaritan between January, 1940, and October, 1948, who on admission had at least minimal rheumatic activity and whose attack was of sixteen weeks' duration or less. Rheumatic activity was arbitrarily graded from minimal, as indicated by elevation of the sedimentation rate, and severe, as indicated by the presence of gross carditis and congestive heart failure. This group was selected to provide information regarding the distribution of the antistreptolysin-O titer in patients with authentic rheumatic fever, which was considered to consist in typical signs of rheumatic heart disease as well as other signs of rheumatic fever.

Group 2

Group 2 consists of 648 consecutive patients with rheumatic fever below the age of seventeen years admitted to the House of the Good Samaritan between January, 1943, and October, 1950. These patients were selected irrespective of rheumatic manifestations, degree of disease activity, cardiac findings and duration of illness. This group provides clinical material for determining the frequency of joint pain as a manifestation of rheumatic fever and for determining the incidence of heart disease among those with joint pain. The distribution of the antistreptolysin-O titer was studied in 227 of the patients in this group who had significant arthritis, who had at least minimal rheumatic activity on admission, and whose attack was of sixteen weeks' duration or less. For purposes of this particular analysis patients were not considered to have significant arthritis unless objective signs involving two or more joints had been witnessed by a physician. The distribution of the antistreptolysin-O titer in these 227 patients was compared with that of the patients with authentic rheumatic fever in Group 1. It should be noted that there is some duplication of the cases included in Group 1 and Group 2.

Group 3

Group 3 consists of 75 patients below the age of seventeen years with definite rheumatoid arthritis (Still's disease) on whom tests for antistreptolysin-O titer were performed. Seventeen of these patients were admitted to the House of the Good Samaritan between January, 1943, and October, 1950, and 58 were admitted to the Children's Hospital between January, 1947, and December, 1953. The distribution of the antistreptolysin-O titer of this group was compared with that of rheumatic-fever patients with significant arthritis in Group 2.

Group 4

Group 4 comprises 92 cases of children below the age of seventeen years, admitted to the Children's Hospital between January, 1950, and December, 1953, with miscellaneous diseases in which joint or extremity pain was a major complaint. The distribution of the antistreptolysin-O titer in these cases was compared with that of the previous groups.

Determination of Titer

Streptolysin-O for use in the antistreptolysin-O test was prepared by the methods of Todd[10] and Hodge and Swift.[11] Since this substance loses its hemolytic activity when it is in the oxidized state, it is necessary to reduce the streptolysin-O before it is used. Before January, 1950, such a reduction was carried out with sodium hydrosulfite; after that date reduction was effected with cysteine hydrochloride according to the method of Rantz and Randall.[12]

Antistreptolysin-O was measured, with slight modification, by the method of Hodge and Swift.[11] The antistreptolysin-O titer is expressed as the reciprocal of the highest serum dilution that completely neutralizes one combining unit of streptolysin-O. The serum to be tested is diluted in a series of tubes in such a way that the logarithms of the titers corresponding to the dilutions in successive tubes increase by 0.10.

Results

Frequency of Joint Pain in Rheumatic Fever

Certain features of the cases composing Group 2 are diagrammatically represented in Figure 1. It is

apparent from this figure that, if cases of chorea are excluded, approximately half the remaining patients with rheumatic fever had significant arthritis and also that half these patients with arthritis had cardiac involvement. Not shown in the figure is the fact that in 243 (94 per cent) of the 257 patients with significant arthritis, joint pain was the initial symptom calling attention to the illness.

Antistreptolysin-O Titer in Group 1

The distribution of the antistreptolysin-O titer of patients with authentic rheumatic fever represented

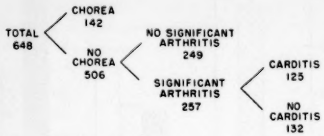

FIGURE 1. *Clinical Features of Cases Composing Group 2.*

in Group 1 is shown in the second and third columns of Table 1 and by the solid line in Figure 2. The data indicate that not 1 out of 208 patients had an antistreptolysin-O titer below 83 and that only 3 (1.5 per cent) had titers below 159 units whereas in 172 cases (over 82 per cent) the titer was 400 units or more.

Antistreptolysin-O Titer in Group 2

The distribution of the antistreptolysin-O titer in 227 cases of rheumatic fever with definite arthritis selected from Group 2 is shown in the fourth and

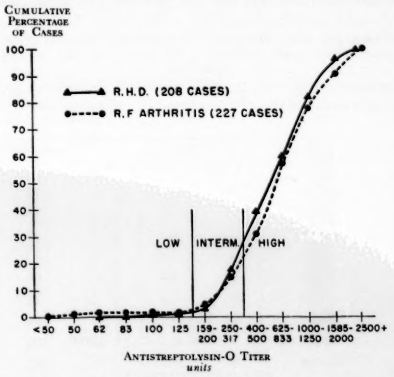

FIGURE 2. *Distribution of Antistreptolysin-O Titer in Group 1 (R.H.D.) and in Cases with Arthritis from Group 2 (R.F. Arthritis).*

fifth columns of Table 1 and by the broken line of Figure 2. It should be noted that 30 of the 257 patients with arthritis in Group 2 (Fig. 1) whose illness was of more than sixteen weeks' duration were not included in this analysis of the antistreptolysin-O titer. It is evident from Table 1 that there were 2 cases with an antistreptolysin-O titer below 50, 1 with a titer of 50, and 1 with 62 units. Altogether, there were only

TABLE 1. *Antistreptolysin-O Titer Distribution (Cumulative Percentage).*

Antistreptolysin-O Titer	Group 1 Cases*		Group 2 Cases†		Group 3 Cases‡		Group 4 Cases§	
	Number	Cumulative Percentage	Number	Cumulative Percentage	Number	Cumulative Percentage	Number	Cumulative Percentage
units								
Below 50	0	0	2	0.9	25	33.3	36	39.1
50	0	0	1	1.3	3	37.3	4	43.5
62	0	0	1	1.8	2	40.0	6	50.0
83	1	0.5	0	1.8	2	42.6	1	51.1
100	1	1.0	0	1.8	5	49.3	4	55.6
125	1	1.5	0	1.8	5	56.0	4	59.8
159-200	4	3.4	7	4.8	5	62.7	16	77.2
250-317	29	17.3	23	15.0	7	72.0	13	91.3
400-500	46	39.4	36	30.8	7	81.3	3	94.6
625-833	43	60.0	60	57.2	9	93.3	2	96.7
1000-1250	47	82.6	47	77.9	3	97.3	1	97.8
1585-2000	29	96.6	29	90.6	0	97.3	2	100.0
Above 2000	7	100.0	21	100.0	2	100.0	0	100.0
Totals	208		227		75		92	

*Rheumatic heart disease.
†Rheumatic fever with arthritis.
‡Rheumatoid arthritis.
§Miscellaneous diseases.

4 cases out of 227 (1.8 per cent) in which the antistreptolysin-O titer was below 159 units. On the other hand, in 193 cases (85 per cent) the titer was

TABLE 2. *Antistreptolysin-O Titer in 227 Cases of Rheumatic Fever with Arthritis (106 with and 121 without Carditis).*

Antistreptolysin-O Titer	Cases with Carditis		Cases without Carditis	
	Number	Cumulative Percentage	Number	Cumulative Percentage
units				
Below 50	1	0.9	1	0.8
50	0	0.9	1	1.7
62	0	0.9	1	2.5
83	0	0.9	0	2.5
100	0	0.9	0	2.5
125	0	0.9	0	2.5
159-200	2	2.8	5	6.6
250-317	8	10.3	15	19.1
400-500	19	28.2	17	33.2
625-833	30	56.4	30	58.1
1000-1250	23	78.0	24	78.0
1585-2000	14	91.2	15	90.5
Above 2000	9	100.0	12	100.0
Totals	106		121	

400 units or more. From Figure 2 it is also evident that the distribution of the antistreptolysin-O titers in

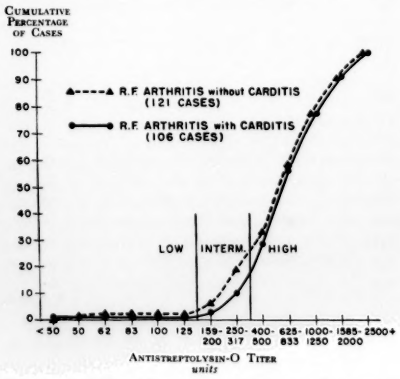

FIGURE 3. *Distribution of Antistreptolysin-O Titer in Cases with Carditis and in Cases without Carditis from Group 2.*

Group 2 patients is very similar to that of Group 1 patients.

The 227 cases with arthritis (Group 2) were divided into two subgroups, those with and those without carditis. The distribution of the antistreptolysin-O titer in each of these subgroups is shown in Table 2 and in Figure 3. The similarity of the distribution curves is apparent. High titers — that is, 400 units or more — were present in 89.7 per cent of the patients with carditis and in 80.9 per cent of those without carditis. Very low titers (less than 159 units)

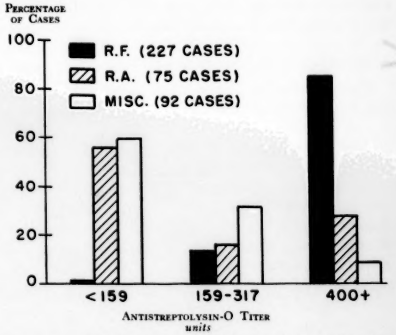

FIGURE 4. *Distribution of Antistreptolysin-O Titer in Rheumatic-Fever Patients with Arthritis (Group 2), Patients with Rheumatoid Arthritis (Group 3) and Patients with Miscellaneous Diseases Associated with Joint Pains (Group 4).*

were present in 2.5 per cent of the patients without carditis and in only 0.9 per cent of those with carditis.

Antistreptolysin-O Titer in Group 3

The distribution of the antistreptolysin-O titer in the 75 cases of rheumatoid arthritis (Group 3) is shown in the sixth and seventh columns of Table 1 and by the shaded bars of Figure 4. It is evident that a third of the patients (25 out of 75) had titers of less than 50 units and that in 56 per cent the titer was less than 159 units. It should be noted, however, that 28 per cent (21 out of 75) had titers of 400 units or more.

Antistreptolysin-O Titer in Group 4

The various diagnoses made in the 92 patients with joint and extremity pain (Group 4) are listed in Table 3. It should be noted that in 18 patients with joint pain and in 9 patients with leg pain the exact cause for the pain was not determined. Also, 7 patients were suspected of having Still's disease, but, since confirmatory follow-up evidence was lacking, these patients have been included in Group 4 rather than in Group 3.

The distribution of the antistreptolysin-O titer of the patients in Group 4 is shown in the last two columns of Table 1 and in the white bars of Figure 4. Here it is to be noted that 39.1 per cent had a titer below 50 and 59.8 per cent below 159 units whereas only 8.7 per cent had titers of 400 units or more.

Influence of Age and Duration of Illness

In a review of the ages of the patients selected for this study, it was noted that rheumatic fever rarely occurred below the age of four years and that rheumatoid arthritis was encountered infrequently in those above twelve years of age. Therefore, to reduce the possible influence of patient age on the differences in distribution of antistreptolysin-O titer observed in the groups with and without rheumatic fever, patients between four and twelve years of age were selected from those with arthritis in Group 2 and from Groups 3 and 4 for further analysis. There was not much difference in the age distribution of the patients in these three selected groups (Fig. 5).

TABLE 3. *Various Miscellaneous Conditions with Joint or Extremity Pain.*

CONDITION	NO. OF CASES
Coxa plana	5
Collagen disease	12
Infectious mononucleosis	5
Joint pain of undetermined etiology	18
Leg pain of undetermined etiology	9
Leukemia	4
Osteomyelitis	6
Poliomyelitis	7
Septic arthritis	6
Still's disease suspected but not proved	7
Traumatic synovitis	10
Tuberculous joints	3
Total	92

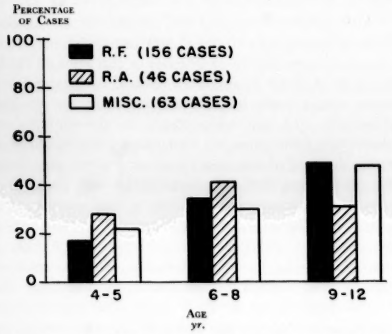

FIGURE 5. *Age Distribution in Selected Cases from Group 2 (Rheumatic Fever with Arthritis), Group 3 (Rheumatoid Arthritis) and Group 4 (Miscellaneous Diseases).*

The distribution of the antistreptolysin-O titers in the three selected groups (Fig. 6) follows a pattern that is similar to that shown for the unselected groups (Fig. 4). Thus, only 2.6 per cent of patients with rheumatic fever had titers below 159 units, whereas 54.3 per cent of those with rheumatoid arthritis and 57.1 per cent of those in the miscellaneous group had titers below 159 units. More than 84 per cent with rheumatic fever, 30 per cent with rheumatoid arthritis, and less than 7 per cent in the miscellaneous group had titers of 400 units or more.

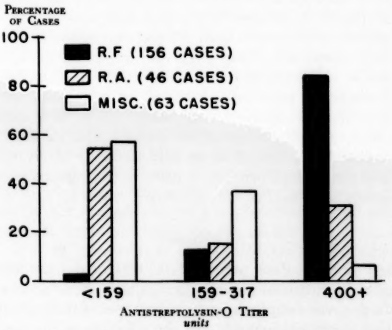

FIGURE 6. *Distribution of Antistreptolysin-O Titer in the Selected Groups of Patients Shown in Figure 5.*

It is to be noted that the patients with rheumatic fever who were chosen for a study of the antistreptolysin-O titer had been ill for only sixteen weeks or less whereas those with rheumatoid arthritis (Group 3) and joint pain from miscellaneous causes (Group 4) were chosen irrespective of the duration of their illness. To reduce the possible influence of duration of illness on the differences in the distribution of the antistreptolysin-O titer observed among the patients

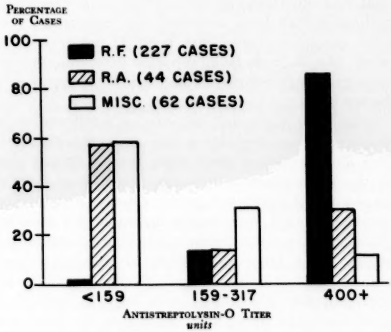

FIGURE 7. *Distribution of Antistreptolysin-O Titer for Patients with Illness of Sixteen Weeks' Duration or Less in Group 2 (Rheumatic Fever with Arthritis), Group 3 (Rheumatoid Arthritis) and Group 4 (Miscellaneous Diseases).*

with and those without rheumatic fever, all patients with illnesses of more than sixteen weeks' duration were excluded from Groups 3 and 4. The distribution of the antistreptolysin-O titer in these selected cases was compared with that for rheumatic-fever patients with arthritis in Group 2, and the results are shown in Figure 7. It is evident that Figure 7 is similar in pattern to Figure 4. Only 1.8 per cent of the patients with rheumatic fever had antistreptolysin-O titers below 159 units, whereas 56.8 per cent of those with rheumatoid arthritis and 58 per cent of those with miscellaneous diseases had titers below 159 units. More than 85 per cent of the patients with rheumatic fever, 30 per cent of those with rheumatoid arthritis and less than 12 per cent of those in the miscellaneous group had titers of 400 or more.

Discussion

From the data presented it is evident that joint pain in rheumatic fever is a frequent manifestation. In this series approximately 50 per cent of the patients had significant arthritis. In the selection of the cases for this series rigid criteria of definite and objective joint signs had to be fulfilled for the case to be accepted as significant arthritis. If less rigid criteria had been followed, the percentage of cases with joint symptoms would have been much higher. Thus, in a recent therapy study of 120 patients in their initial attack of rheumatic fever admitted to the House of the Good Samaritan since 1949, 74 per cent had objective signs of arthritis.[5] If cases with arthralgia had been included, the proportion with joint symptoms would have been 92 per cent. This study, like the study being reported here, was confined to patients without chorea and below the age of seventeen years.

Joint pain is not only a frequent manifestation of rheumatic fever but also a very early manifestation. The data presented above show that in 94 per cent of the 257 patients with arthritis in Group 2, joint pain was the initial symptom. Finally, it should be emphasized that joint pain is an important manifestation of rheumatic fever since heart damage develops in a large proportion of rheumatic-fever patients with joint symptoms. In the present study approximately half those with arthritis had signs of carditis. In brief, then, joint pain in rheumatic fever is a frequent, early and significant manifestation, and it is of considerable diagnostic importance provided it can be differentiated from joint pain from other causes.

In a study of the possible value of the antistreptolysin-O titer in the differentiation of the joint pain of rheumatic fever from that of other causes, observations were made on a group of rheumatic-fever patients with significant arthritis (Group 2). Although the diagnosis of rheumatic fever could not be made with absolute certainty in this group of patients on the basis of arthritis alone, there is good reason to believe that they were suffering from rheumatic fever for the following reasons: the distribution of the antistreptolysin-O titer was similar to that for the Group 1 patients in whom the diagnosis of rheumatic fever was conclusively proved by the presence of rheumatic heart disease; approximately half the patients with arthritis in Group 2 had carditis, and the distribution of the antistreptolysin-O titer was similar for those with and those without carditis; and the cases of arthritis in Group 2 were clinically diagnosed as rheumatic fever by members of the staff of the House of the Good Samaritan, who have had considerable experience in the problem of rheumatic fever and rheumatic heart disease.

Comparison of the distribution of the antistreptolysin-O titer in the groups with and without rheumatic fever shows that 85 per cent of the patients with rheumatic fever, 28 per cent of those with rheumatoid arthritis, and 8 per cent of those in the miscellaneous group had titers of 400 units or more. It is apparent from these data that, if an attempt had been made to differentiate the joint pain of rheumatic fever from that of rheumatoid arthritis and from that of the miscellaneous diseases in Group 4 on the basis of a high antistreptolysin-O titer alone (400 units or more), one would have missed 15 per cent of the patients with rheumatic fever and would have included 28 per cent of those with rheumatoid arthritis and 8 per cent of those with miscellaneous diseases among the patients with rheumatic fever.

Although 8 per cent of the patients in the miscellaneous group had titers of 400 units or more, it is apparent from the list of diseases in this group (Table 3) that in most cases other clinical and laboratory signs would have helped prevent confusion in the diagnosis. On the other hand, in rheumatoid arthritis the joint pains are sometimes indistinguishable from those of rheumatic fever, and there are often no other signs that differentiate the two diseases.

In the cases of arthritis with a high antistreptolysin-O titer in which the differentiation of rheumatic fever and rheumatoid arthritis may be difficult, a consideration of the age distribution and the relative frequency of the two diseases may aid in the diagnosis.

Rheumatic fever is rare under the age of four years and extremely rare under the age of three years, whereas rheumatoid arthritis is not uncommon in very young children. Thus, in the patients with rheumatic fever observed in the present study (Groups 1 and 2) there were only 3 (less than 1 per cent) below the age of four years, only 1 of whom was less than three years of age. In contrast, of the 75 patients with rheumatoid arthritis in Group 3, 29 (39 per cent) were under the age of four, and 14 (19 per cent) under the age of three years.

We are not aware of any study showing the relative frequency of rheumatic fever and rheumatoid ar-

thritis in childhood. Although hospital-admission statistics may be misleading, they may be utilized to furnish a rough index of the relative frequency of these two diseases. During the period from 1941 to 1953 there were 94 children with rheumatic fever (exclusive of those with chorea) and 31 with rheumatoid arthritis (Still's disease) four years of age or older admitted to the Children's Hospital. If these admission rates can be used as an index of the relative frequency of rheumatic fever and rheumatoid arthritis in childhood, and if the data on the antistreptolysin-O titer in the present study can be accepted as indicating the relative frequency of high titers in the two diseases, it appears that in a patient between the ages of four and sixteen years with objective arthritis and an antistreptolysin-O titer of 400 units or more the chances are considerably greater that the diagnosis is rheumatic fever rather than rheumatoid arthritis. It must be noted, however, that since some patients with rheumatoid arthritis have titers of 400 units or more, objective signs of arthritis and a high antistreptolysin-O titer alone are insufficient for a conclusive diagnosis of rheumatic fever.

In connection with the observation of antistreptolysin-O titers of 400 units or more in 8 per cent of the patients with miscellaneous diseases (Group 4), it should be noted that this incidence of high titer is similar to that observed in healthy children.[13-15] Thus, in a study previously reported from the House of the Good Samaritan,[13] 57 (8 per cent) of 698 apparently healthy children in the Boston area were found to have antistreptolysin-O titers of 400 units or more.

Although a high antistreptolysin-O titer is quite helpful in confirming a diagnosis of rheumatic fever, a very low titer is even more helpful in excluding rheumatic fever. Thus, if an antistreptolysin-O titer of less than 159 units had been used to exclude active rheumatic fever in the Group 2 patients with arthritis, only 4 cases out of 227 (1.8 per cent) would have been incorrectly classified as not being rheumatic fever. Hollinger,[9] in reviewing 1339 cases of rheumatic fever collected over a twenty-year period from the United Kingdom and this country, found only 11 patients with titers of 50 units or less. In the present series of 435 cases of rheumatic fever (Groups 1 and 2 combined) there were only 3 patients with antistreptolysin-O titers of 50 units or below, a result markedly similar to that of Hollinger's study. However, we have considered any titer below 159 units as low, because the distribution curve for antistreptolysin-O titer in Groups 1 and 2 (Fig. 2) shows a sharp change in direction at this level. Even then, only 1.8 per cent of the cases would have been incorrectly classified as nonrheumatic. This incidence of low titers, as pointed out by Hollinger, compares favorably with data on false-negative findings in serologic tests in untreated secondary or tertiary syphilis.[16]

A statistical analysis of the data in Table 1 for Groups 2, 3 and 4 showed that the differences in distribution of the antistreptolysin-O titer in these three groups would have a probability of less than 0.001 of occurring by chance.

In spite of this apparent statistical validity the possibility was considered that the differences observed among the three groups were due to variables such as differences in age of the patients and differences in duration of illness. Although the role of these possible factors cannot be entirely eliminated because of the retrospective nature of this study, the additional studies that have been described in which patients of fairly comparable age and with illness of fairly comparable duration were selected for further analysis suggest that these factors did not have an important effect on the results.

It is of interest that the distribution of the antistreptolysin-O titer is essentially the same for the patients with carditis and those without carditis in Group 2. Hence, the height of the antistreptolysin-O titer, although useful in the diagnosis of rheumatic fever, is not helpful in predicting the development of heart damage.

Summary and Conclusions

Data on the frequency, early appearance and importance of joint pain as a manifestation of rheumatic fever in 648 consecutive patients below the age of seventeen years admitted to the House of the Good Samaritan between 1943 and 1948 are presented. The results indicate that, if cases of chorea are excluded, 50 per cent of the remaining patients had significant arthritis, that in 92 per cent of the rheumatic-fever patients with arthritis, joint pain was the earliest symptom, and that 50 per cent of the patients with arthritis had cardiac involvement.

Data on the distribution of the antistreptolysin-O titer of four different groups (208 cases of authentic rheumatic fever with carditis, 227 cases of rheumatic fever with arthritis, 75 cases of rheumatoid arthritis and 92 cases of miscellaneous diseases with joint pain), all patients being below the age of seventeen years, admitted to the House of the Good Samaritan or the Children's Hospital are also reviewed.

Distribution of the antistreptolysin-O titer in 227 rheumatic-fever patients with arthritis was very similar to that of 208 patients with rheumatic fever regarded as authentic because of the presence of cardiac involvement. Furthermore, the distributions of the antistreptolysin-O titer of the subgroups with and without carditis in the rheumatic-fever patients with arthritis were similar.

Eighty-five per cent of the patients with rheumatic fever, in contrast to 28 per cent of those with rheumatoid arthritis and 8 per cent in the miscellaneous group, had antistreptolysin-O titers of 400 units or more. On the other hand, 56 per cent of the patients

with rheumatoid arthritis, 60 per cent with miscellaneous diseases and only 1.8 per cent with rheumatic fever had titers below 159 units.

A study of selected groups of patients of fairly comparable age and with illnesses of fairly comparable duration suggests that neither patient age nor duration of illness had a significant effect on the differences in distribution of the antistreptolysin-O titers observed among the patients with rheumatic fever, rheumatoid arthritis and miscellaneous diseases.

Although definite information regarding the relative frequency of rheumatic fever and rheumatoid arthritis in childhood is not available, the admission data from the Children's Hospital suggest that rheumatic fever is encountered much more frequently than rheumatoid arthritis in children above the age of four years.

It is concluded that joint pain is a frequent, early and important manifestation of rheumatic fever. It is also concluded that the antistreptolysin-O titer is a helpful laboratory test in the differentiation of joint pains of rheumatic fever from those of rheumatoid arthritis and miscellaneous diseases with joint pain. Joint pain with high antistreptolysin-O titer (400 units or more) is consistent with, though not diagnostic of, rheumatic fever. The present study indicates that in patients between the ages of four and sixteen years the combination of joint pain and high antistreptolysin-O titer is encountered much more frequently in rheumatic fever than in rheumatoid arthritis. Antistreptolysin-O titers of less than 159 units in patients with joint pain may be regarded as an important negative exclusion index for the presence of active rheumatic fever. This study also shows that the height of the antistreptolysin-O titer cannot be used in the prediction of heart damage.

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FOLLOW-UP STUDIES OF ILIOFEMORAL ARTERIAL RECONSTRUCTION IN ARTERIOSCLEROSIS OBLITERANS*

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BOSTON AND WEST ROXBURY

RECENT surgical intervention in the treatment of localized peripheral arterial blockage resulting from arteriosclerosis obliterans has had varied results. Removal of the intra-arterial block en masse by thromboendarterectomy was originated by dos Santos.[1] Applied to the femoral artery, its most recent modification by Cannon and Barker[2] has proved 87 per cent effective. The insertion of vessel grafts — arterial and venous, autogenous and homologous — has, according to recent reports, shown an effectiveness ranging from 35 to 75 per cent[3-5] for femoral occlusion. This study is designed to add results to those already reported in the literature so that proper indications for this type of arterial reconstruction may eventually be delineated.

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Definition of Material

The report covers primary arterial reconstruction in the iliofemoral arterial trunk. Specifically omitted are aortic reconstructions. Late secondary reconstructions performed on limbs in which a primary reconstruction, initially successful, has later closed are, for purposes of this study, not considered separate operations.

Thirty-one operations were performed on 29 male patients, 2 patients undergoing the operation on both

extremities. The operations were performed at the Veterans Administration Hospitals in Boston and West Roxbury between November, 1952, and February, 1955. The follow-up period was from two to twenty-nine months and was complete to April 1, 1955.

The ages varied from thirty-two to seventy-three years, the mean age being fifty-eight years.

Presenting Symptom

The major presenting symptom was intermittent claudication, present in 22 extremities, varying in distance of onset, but severe enough in each case to prompt the patient to seek medical aid. The other presenting symptoms, indicative of more severe ischemia, are grouped as follows: objective evidence of tissue breakdown (6 extremities); and rest pain (3 extremities).

Concomitant Disease

Seven patients had diabetes. Seven of the patients had had cerebrovascular accidents or myocardial infarctions, with good functional recovery, or had angina of mild degree.

Twelve patients had symptoms of intermittent claudication in the contralateral extremity, and 3 had had contralateral lumbar sympathectomy. In 1 patient an arteriosclerotic fusiform abdominal aneurysm had previously been resected and grafted with postoperative block of one common iliac artery. Seven months later this was bypassed by a splenofemoral arterial homograft.

Arteriograms

The *sine qua non* of consideration for grafting was failure of palpable pulsation below the iliac or femoral areas. In such situations an aortogram or arteriogram was taken. If a block was found and the popliteal artery demonstrated to be patent below, it was considered anatomically feasible to attempt surgery. If the arteriogram showed no patent distal vessel of sufficient caliber for grafting, no reconstructive procedure was advised. The rationale of this conclusion is borne out by the experience of Dye, Olwin and Julian[6] and by our own earlier studies, which demonstrated that in several cases showing no open popliteal artery by arteriography satisfactorily performed, surgical exploration consistently found the popliteal artery to be occluded.

The blocks were distributed as follows: iliac, 6; common femoral, 1; and superficial femoral, 27. Since some legs showed more than one block, there were 34 blocks in 31 legs.

A survey of the aortograms and arteriograms performed at the West Roxbury Veterans Administration Hospital from October, 1953, to April, 1955, demonstrated 25 patent popliteal arteries in 32 roentgenologic examinations. Of these, 20 patients are included in the present group, and 1 is preoperative at present. In 2 of the remaining 4 cases the patients were considered to have too much cardiac and pulmonary disease, in 1 a vasospastic element with peripheral pulses intermittently present was thought to exist, and in 1 the symptoms were considered due to concomitant venous stasis. This incidence (78 per cent) of potentially operable lesions has been noted before by us and is higher than that reported by others.

Operation

In the 31 extremities, the types of reconstruction were 16 arterial homografts, 12 saphenous-vein autografts, 1 superficial-femoral-vein autograft and 2 thromboendarterectomies. The details of operative technic have been previously reported.[7] Some modifications have been made since then. In the last half of the patients, for instance, end-to-side anastomoses between the graft and the host artery have been made when possible because no collaterals are divided, because the operator may select the optimal location in the circumference of the vessel for the site of anastomosis and because easier control of the size of the anastomotic lumen is arranged. Except for the first few cases, the blocked segment has not been removed, a feature that simplifies the surgical technic. There may even be a contraindication to removal in the observation of Dye, Olwin and Julian[6] that nonligated bypassed segments may form postoperative hematomas in varying degrees, demonstrating some measure of residual function.

Table 1. *Operative Complications of 31 Arterial Reconstructions.*

Complication	No. of Cases
Skin slough	2
Hemorrhage	4
Local sepsis	1
Early thrombosis	3
Total	10

The homologous arterial grafts used were prepared by quick-freezing technic and sterilized by irradiation as described by Gross et al.[7] The autogenous saphenous-vein grafts were removed at the time of surgery from the same leg.

Results

There were no operative or hospital deaths. There has been only 1 later death — in a patient who was found dead in bed at home eight months postoperatively, having had no cardiac symptoms at the time of surgery.

The operative complications are listed in Table 1. There were 6 immediate (within twenty-four hours) reoperations. These were performed for thromboses and hemorrhages in 2 cases each and in 2 cases in

which there was doubtful arterial inflow immediately after operation but re-exploration showed patent grafts.

The 2 thromboendarterectomies were performed early in the series, and both reoccluded within the period of hospitalization. Since then this procedure has been used only as an adjunct to grafting.

Of the 29 patients who had grafts inserted, all but 3 left the hospital with a patent graft. Of the 16 arterial grafts, 9 have closed, all within seven months (Table 2). Of the 13 autogenous vein grafts, 8 have reoccluded — 6 within six months and the other 2 at eight and nine months.

In the 19 cases of closure, 4 limbs were improved, 9 showed no change, and 6 were made worse as compared with the preoperative status (all 6 patients later came to amputation). The operations in these 6 were performed in patients presenting necrosis or rest pain. We have subdivided them into three groups; 2 patients who would have required amputation anyway; 3 who probably would have required amputation; and 1 who would not have needed amputation. In the last patient the poor result was considered to be due to a technical error in that the deep femoral artery was ligated to effect a more convenient end-to-end anastomosis. When the graft closed six months later the patient had no source of collateral circulation to his lower leg. The use of the end-to-side anastomosis obviates the temptation to make such an error again.

Of the 29 grafts, 7 were performed within the six months immediately before the termination of the study (Table 3). At present there are 5 patent grafts in this group. Of the 22 grafts followed for six months or more, 2 of 9 arterial grafts maintained patency, and 5 of 13 venous grafts were open, giving a rate of 32 per cent for patency in those followed for over six months.

TABLE 2. *Follow-up Results of 31 Arterial Reconstructions.*

PROCEDURE	NO. OF CASES	GRAFT CLOSED IMMEDIATELY	GRAFT CLOSED LATER
		NO. OF CASES	NO. OF CASES
Thromboendarterectomy	2	2	0
Venous autograft	13	1	7
Arterial homograft	16	2	7
Totals	31	5(19%)	14(45%)

TABLE 3. *Results in 24 Patients with Arterial Reconstructions Followed for More than Six Months.*

PROCEDURE	TOTAL NO. OF CASES	EARLY CLOSURE	LATE CLOSURE
		NO. OF CASES	NO. OF CASES
Thromboendarterectomy	2	2	0
Venous autograft	13	1	7
Arterial homograft	9	2	5
Totals	24	5(21%)	12(50%)

TABLE 4. *Correlation of Age with Patency in 24 Arterial Reconstructions Followed for More than Six Months.*

DECADE	GRAFT OPEN	GRAFT CLOSED
	NO. OF CASES	NO. OF CASES
yr.		
31-40	0	3
41-50	1	2
51-60	0	5
61-70	5	6
71-80	1	1

TABLE 5. *Correlation of Surgeon's Opinion with Patency of the Graft in 24 Arterial Reconstructions Followed for More than Six Months.*

SURGEON'S OPINION	GRAFT OPEN	GRAFT CLOSED
	NO. OF CASES	NO. OF CASES
"Satisfied"	3	12
"Dissatisfied"	4	5

DISCUSSION

The most important question that remains unanswered is the reason for the delayed closures. The first six or seven months seems to be the critical time, since in 12 of the 14 grafts that have closed this occurred within seven months. The other 2 closures occurred at eight and nine months.

TABLE 6. *Correlation of Type of Anastomosis with Patency in 24 Arterial Reconstructions Followed for More than Six Months.*

TYPE OF ANASTOMOSIS	GRAFT OPEN	GRAFT CLOSED
	NO. OF CASES	NO. OF CASES
End-to-end & end-to-end	6	9
End-to-side & end-to-end	1	3
End-to-side & end-to-side	0	3

An analysis of the factors of age of patient, technical and anatomic features, length of graft and patency of the lower arterial tree has been made. No correlation between patency and age of patient could be established (Table 4).

A satisfactory anastomosis and anatomic lie are probably the two most important items within the operative procedure, but the longest period of patency observed (twenty-five months) occurred in a graft estimated by the operator to be too short, the anastomosis having been performed with the knee flexed. The degree of satisfaction of the surgeon as judged from the operative note and additional record entries shows no correlation with graft patency (Table 5).

The type of anastomosis also fails to offer any correlation (Table 6).

The length of the implanted segment was equally distributed above and below 20 cm. in the grafts remaining patent, although there appears to be a tendency for twice as many grafts over 20 cm. long to close (Table 7).

TABLE 7. *Correlation of Length of Reconstruction with Patency in 24 Arterial Reconstructions Followed for More than Six Months.*

LENGTH OF RECONSTRUCTION	GRAFT OPEN	GRAFT CLOSED
	NO. OF CASES	NO. OF CASES
cm.		
<10	1	2
11-15	2	2
16-20	1	2
21-30	2	6
>30	1	5

Peripheral-pulse return may be slow and once took as long as ten days, but the majority of patients showed at least one palpable pulse below the reconstruction within four hours. There was no correlation between early return of peripheral pulses after the procedure and persistence of patency (Table 8).

TABLE 8. *Correlation with Rapidity of Pulse Return in 24 Arterial Reconstructions Followed for More than Six Months.*

INTERVAL BEFORE PULSE RETURN	GRAFT OPEN	GRAFT CLOSED
	NO. OF CASES	NO. OF CASES
<24	4	14
>24	3	2
Never	0	1

Closer analysis within the first twenty-four hours shows a slight — but inconclusive — tendency for the patent grafts to have peripheral pulsations at the close of the operation or shortly thereafter. Similarly, there was no correlation between the degree of objective re-establishment of circulation (number of pulses and degree of oscillations returning) and the persistence of patency (Table 9). Much has been written of the capacity of the distal circulatory tree to transport an adequate volume of blood, especially in the selection of patients for grafting, but adequate return of pulses and oscillations did not protect against closure in this small group.

TABLE 9. *Correlation of "Runoff Area" with Patency in 24 Arterial Reconstructions Followed for More than Six Months.*

STATUS OF PULSE	GRAFT OPEN	GRAFT CLOSED
	NO. OF CASES	NO. OF CASES
No peripheral pulses	0	1
Popliteal pulses only	2*	1
1 pedal pulse	3	6
Both pedal pulses	2	9

*1 patient had previous amputation below knee.

Although many of the grafts that closed showed narrowing of one or both anastomoses by postoperative arteriogram (Fig. 1), some of those staying open have shown similar deformities, and those with no visible site of anastomosis have not been exempt from closure.

FIGURE 1. *Postoperative Arteriogram, Showing Narrowing of Anastomosis.*

Specimens of 4 grafts (3 arterial homografts and 1 venous autograft) were obtained shortly after thrombosis occurring between two and a half and seven months after operation. They were obtained from points of the grafts somewhat distant from the anastomoses. In the 3 arteries thrombi of varying ages were demonstrable microscopically. Well developed organization in a thrombus could be seen with partial coverage by endothelium and more recent thrombus overlying this, producing luminal occlusion (Fig. 2). The vein showed only one area of old thrombosis. The final total occlusion in the homograft is apparently not a sudden process, but rather the result

of a gradual or recurrent one. Whether it is caused by a gradual progression of the original disease or a reaction to the graft is unknown. There was no evidence of cholesterol deposits in any of the specimens.

The report has been made without reference to indications for such operations in the future. If "creeping" thrombosis is an important mechanism, particularly in the homografts, it is useless to concentrate on further improvement of operating-table technics. A continual search must be made for better forms of graft. A trial of cloth prostheses, when they can be successfully fashioned for these smaller arteries, must be made to ascertain if such processes do not occur in them. A revival of thromboendarterectomy may be around the corner if confirmation of the high success rate reported by Cannon and Barker[2] is forthcoming from other clinics.

FIGURE 2. *Specimen of Graft, Showing Occlusion of the Lumen.*

Patients with necrosis or rest pain can be benefited, since 3 grafts of 9 such patients are still patent. Although amputations were not completely averted in 2 cases, lower amputations than would previously have been possible have been followed by healing by first intention. One of them was a Syme amputation, which was functional until graft closure five months later necessitated higher amputation. The other was an amputation below the knee after necrosis of a previous Syme stump. This level of amputation was undoubtedly made possible by a homologous arterial graft inserted as a preliminary to it.

Accordingly, despite the frequency of later failure of these reconstructions we still advise the procedure for any person who is really disabled by ischemic symptoms from the normal activity of his age group. The use of lumbar sympathectomy as a preliminary measure is wise as a protection against later graft closure.

SUMMARY

Follow-up studies of attempts at arterial reconstruction in 29 patients and 31 extremities are reported.

Thromboendarterectomies in 2 cases occluded within the period of hospitalization.

Of 29 patients with grafts inserted, 26 left the hospital with a patent graft. Of 16 arterial grafts, 9 had closed at the follow-up examination, and of the 13 venous grafts, 8 had closed. Of the 14 grafts closing after the patient left the hospital, 12 did so within the first seven months.

At present, there are 12 grafts functioning — 7 arterial and 5 venous. Of these 12, 7 have been followed over six months.

The various factors that may contribute to late closure offer no substantial clue to the cause. The finding of disseminated, partially occluding organized thrombi in the occluded grafts was striking.

Since this paper was submitted for publication 3 more grafts have closed as follows: a 45-cm. end-to-side by-pass homograft closed one year after insertion; a 30-cm. end-to-side by-pass homograft closed six months after insertion; and a 14-cm. resection and end-to-end homograft closed two and a half years after insertion. The total number of known closed grafts in the series of 31 is thus 22, or 70 per cent.

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FEVER AND ANEMIA IN RENAL CANCER*

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BOSTON

A SURVEY of 36 proved cases of renal cancer has been made to determine the importance of fever and anemia as diagnostic signs in this disease. All patients underwent operations: nephrectomy in 35 and exploration and biopsy in 1. The histologic diagnosis, in every case, was consistent with cancer of the tubular epithelium. Various names have been applied to this neoplasm, including Grawitz's tumor, hypernephroma, clear-cell carcinoma and renal-cell or renal-tubular carcinoma.

Table 1. *Data in 36 Cases of Renal-Tubular Carcinoma.*

Datum	Age	No. of Patients
	yr.	
Youngest patient	32	
Oldest patient	84	
Average age	56	
Sex:		
Male		23
Female		13
Side of body affected:		
Right		10
Left		16

Table 2. *Chief Complaints.*

Chief Complaint	No. of Cases
Hematuria	10
Lassitude	6
Weight loss	5
Flank pain	5
Fever	2
Abdominal pain	2
None (abdominal mass discovered incidentally on roentgenogram)	2
None (palpable mass discovered incidentally)	2
None (incidental discovery on routine urinalysis)	1
Pain in left thigh	1

Results

Our findings are summarized in Tables 1 to 7. Two of the 36 patients presented otherwise unexplained fever as a chief complaint (Table 2). Eight others had fever as a symptom or sign (Table 3). The daily maximum temperatures varied in these cases from 100 to 102°F. In 9 of the 10 patients fever disappeared after nephrectomy. The exception (Case 1) was a man in whom hepatic metastases were proved at operation.

Table 3. *Symptoms.*

Symptom	No. of Cases
Weight loss	17
Lassitude	14
Flank pain	14
Hematuria	12
Fever	10
Abdominal pain	6
None (incidental discovery of abdominal mass on roentgenogram)	2
None (incidental discovery of palpable mass)	2
None (incidental discovery on routine urinalysis)	1
Pain in left thigh	1

Pronounced anemia (hemoglobin of less than 11 gm. per 100 cc.) was found in 9 cases (Table 5). Anemia was corrected by transfusion during the operative period and did not recur as long as the patients remained free of other signs of tumor recurrence. Lassitude, which was more common (Table 3) than the objective findings of anemia, was a complaint in 14 patients.

Table 4. *Abnormal Physical Findings.*

Physical Finding	No. of Cases
Palpable mass	16
No abnormal finding detected	10
Pallor	4
Wasting	4
Supraclavicular lymph nodes	1
Swelling of left scrotum	1

No positive correlation could be established (Table 7) between presence of fever or anemia and pathological demonstration of invasion of renal veins or renal pelvis or across the renal capsule.

The following cases are typical:

Case Reports

Case 1. (N. E. C. H. 93819). A 47-year-old man had complained of fever and lassitude for 4 months. Finally, he

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passed blood clots in the urine. An intravenous pyelogram showed no function in the right kidney. Retrograde study disclosed a large tumor of the upper pole of the right kidney. At thoracoabdominal nephrectomy an 8-cm. cancer that had invaded the renal vein and renal pelvis was found. There were nodules in the liver, biopsy of which demonstrated cancer similar to that occurring in the kidney. Fever persisted after the operation.

Microscopical specimens were of interest in that different parts of the tumor contained fields suggesting anaplastic tubules (Fig. 1), hypernephroid formations (Fig. 2), and clear-cell carcinoma (Fig. 3).

TABLE 5. *Laboratory Data.*

DATUM	NO. OF CASES
Hemoglobin level:	
5-7 gm. per 100 cc.	1
7-9 gm. per 100 cc.	3
9-11 gm. per 100 cc.	5
11-13 gm. per 100 cc.	8
Over 13 gm. per 100 cc.	17
White-cell count:	
Under 10,000	23
Over 10,000	9
Differential count:	
Under 80% neutrophils	31
Over 80% neutrophils	2
Blood sedimentation rate*:	
Under 20 mm. per hr.	10
Over 20 mm. per hr.	26
Urinalysis:	
Albuminuria	3
Microscopical hematuria	13
Pyuria	1

*Westergren method.

TABLE 6. *Pathological Findings in All Cases.*

PATHOLOGICAL OBSERVATION	NO. OF CASES
Invasion of renal veins	15
Invasion of renal pelvis	13
Transcapsular invasion	7
Transcapsular invasion & local extension to other structures	5
Positive regional lymph nodes (8 lymphadenectomies)	1

CASE 2. (N. E. C. H. 78363). A 47-year-old woman had been treated unsuccessfully for anemia and fever for 6 months. Though no distortion of the renal pelvis was apparent in the pyelogram a large mass was seen in the upper pole of the left kidney. After thoracoabdominal nephrectomy, fever and anemia did not recur (Fig. 4). Although no invasion of the renal vein could be found in the specimen, she returned to the hospital 6 months later with tumor recurrence in the superior vena cava. Sections of the kidney showed a typical clear-cell carcinoma, separated from normal kidney by a fibrous, capsulelike structure.

TABLE 7. *Pathological Findings in 10 Cases with Fever as a Presenting Symptom.*

PATHOLOGICAL OBSERVATION	NO. OF CASES
Invasion of renal veins	6
Invasion of renal pelvis	4
Transcapsular invasion	2
Transcapsular invasion & extension to other structures	3
Invasion of regional lymph nodes	1
Blood-borne metastasis to liver	1

DISCUSSION

Our data suggest that kidney cancer may be an important differential diagnosis in cases of otherwise unexplainable fever or anemia. The reason for common occurrence of these signs in carcinoma of the renal-tubular epithelium is not clear but is probably related to its tendency to vascularity (Fig. 5) and peculiar affinity for the venous system.

FIGURE 1. *Section from the Renal Tumor in Case 1, Showing Disorganized Tubules (X22).*

Israel,[1] in 1911, found fever in 18.2 per cent of 146 cases of kidney cancer. Like ourselves, he could not correlate its occurrence with pathological find-

ings of renal-vein involvement, transcapsular invasion or invasion of adjacent structures. Creevy[2] reported fever in 2 of 17, Young and Davis[3] in 4 of 44, and Griffiths and Thackray[4] in 12 of 103 cases.

FIGURE 2. *Section from the Renal Tumor in Case 1, Showing Hypernephroid Formations (X21).*

Cases in which the fever disappeared after nephrectomy have been described by Israel[1], Catlin et al.,[5]

FIGURE 3. *Section from the Renal Tumor in Case 1, Showing Clear-Cell Carcinoma (X75).*

Zádor,[6] Griffiths and Thackray,[4] Rowlands[7] and Sumner.[8]

SUMMARY AND CONCLUSIONS

Fever was found in 10 of 36 patients operated on for carcinoma of the renal-tubular epithelium. In 2 of these, unexplained fever was the chief complaint.

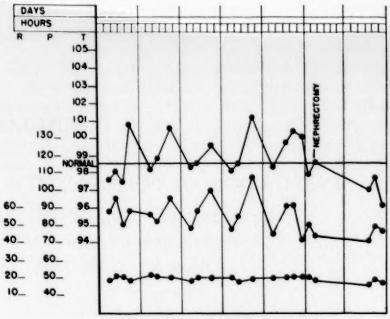

FIGURE 4. *Clinical Course in Case 2.*

Fever was found to have no relation to pathological findings of invasion of the renal vein, renal pelvis or adjacent structures. In 9 of the 10 patients, fever

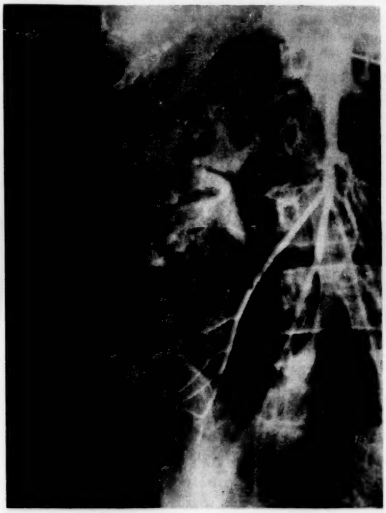

FIGURE 5. *Aortogram in a Proved Case of Renal Tubular Carcinoma.*

disappeared after nephrectomy. In the case in which it persisted, hepatic metastases were found at surgery.

Significant anemia occurred in 9 of the 36 patients.

Fever or anemia occurring in renal cancer does not necessarily indicate inoperable distant metastasis and does not contraindicate nephrectomy in an attempt at palliation or cure.

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SPECIAL ARTICLE

EVALUATION OF POLIOMYELITIS VACCINATION IN MASSACHUSETTS*

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BOSTON

IT is ironic that Massachusetts should have had its largest epidemic of poliomyelitis just before the time when poliomyelitis vaccine was to become available in sufficient quantities to protect the whole of the younger population. However, this furnished an unprecedented opportunity to evaluate the effectiveness of the vaccine in an epidemic situation. At the suggestion and with the financial assistance of the National Foundation for Infantile Paralysis, a special study was undertaken. Since the regular personnel of the Department were devoting their entire time to matters connected with the epidemic itself, it was necessary to obtain special field and office personnel to conduct the study.

The 1955 Epidemic of Poliomyelitis

A few facts about the epidemic are necessary for a proper understanding of the possible effects of the vaccine.

The State was set for an epidemic year because it had been six years since the last epidemic and because just before 1949 the annual number of births had increased to about 100,000 per year, whereas before World War II the number had been nearer to 60,000 per year. In the interim since the 1949 epidemic there had been some fairly high years, but in both 1951 and 1954 many of the cases were undoubtedly due to confusing viruses.

The 1955 epidemic began in Boston during the first week in July and spread immediately to contiguous communities. Since the rapid upward swing began three or four weeks earlier than usual, it was predicted that the peak would occur in Boston in the first or second week in August and that the peak for the State would follow within a week or two. These predictions were based upon the shape of the epidemic curve in Massachusetts in previous years of high incidence. Actually, the peak in Boston occurred in the week ending August 12, and that for the State in the week ending August 19 (Fig. 1). It was at this date that the special study was organized.

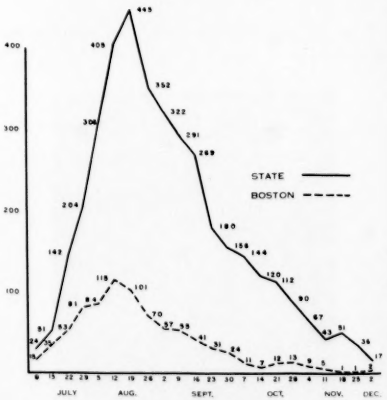

FIGURE 1. *Weekly Incidence of Poliomyelitis for Massachusetts and Boston (1955).*

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Types of Cases

The outbreak was due almost entirely to Type 1 virus. A minimum number of cases were caused by other agents. Other infections were highly prevalent in 1954, the year of the field trials. They had also caused confusion in 1948 and 1951. In all three years the usual ratio of 60 per cent paralytic and 40 per cent nonparalytic cases was reversed. This reversal is usually the first evidence of the presence of confusing viral infections.

There was some fluctuation in the percentage of nonparalytic cases from month to month. In July only 33.9 per cent of the reported cases were nonparalytic. In August the figure rose to 38.1 per cent, and in September it declined to 36.1 per cent. There was a fall in October to 31.9 per cent and a rise in November to 37.9 per cent.

It is difficult to determine the reason for these fluctuations. At first glance it appears that awareness of the presence of poliomyelitis increased among both parents and physicians during the months of high incidence, and it may be that minor symptoms were carefully observed at that time. The second rise, in November, could not be explained on this basis. On the other hand, other viruses causing similar symptoms may have played a minor part. Laboratory studies yet to be carried out may throw some light on this problem. The general low figure (36.3 per cent) of nonparalytic cases is evidence that confusing viruses were low in incidence in 1955.

The percentage of bulbar cases also fluctuated from month to month. In July 16.8 per cent of reported cases were bulbar, this figure rising in August to 19.8 per cent. Thereafter, the proportion dropped to 15.9 per cent in September, 13.9 per cent in October and 14.0 per cent in November. There was a rise in the bulbar cases over previous years, 17.4 per cent of all cases being reported as bulbar. In 1945, 16.5 per cent was recorded, but ordinarily the figure is much nearer 10 per cent.

Age and Sex

The 1955 epidemic was characterized by a reversal of the downward trend in the percentage of cases in persons under five years of age. Up to 1918 about 65 per cent of patients were under five years. By 1930 the proportion had dropped nearer to 33 per cent. In recent years it had been regularly about 19 per cent. In 1955 the figure rose to 30.6 per cent (Table 1.)

In the group five to nine years of age the trend had been different. Beginning at about 19 per cent up to 1918, the figure had risen to nearer 33 per cent by 1930, falling in recent years to about 25 per cent. In 1955 the figure remained at 25.6 per cent. No doubt, there would have been a rise in this age group if many of the older children had not been exposed and become immune during the 1949 epidemic, and if nearly a third had not received one or more doses of vaccine in 1954 and 1955.

The rise in percentage under five years necessarily decreased the proportion in older age groups. In recent years the group ten to fourteen years of age had accounted for about 19 per cent of all cases. The figure dropped to 11.2 per cent in 1955, perhaps because this age group had gone through the 1949 epidemic.

Those over fourteen years of age have constituted

Table 1. *Cases of Poliomyelitis by Age, Sex and Type of Involvement (Massachusetts, 1955).*

Age	Bulbar Involvement		Paralytic Cases		Nonparalytic Cases		Type of Involvement Not Stated	Totals	Percentage for Each Age
	Males	Females	Males	Females	Males	Females	No. of cases		
yr.									
0-4	93	58	381	269	209	113	45	1168	30.6
5-9	119	77	207	142	243	148	42	978	25.6
10-14	52	39	86	61	90	74	25	427	11.2
15-19	28	10	55	49	65	26	15	248	6.5
20-24	14	16	40	57	37	62	19	245	6.4
25-29	23	28	67	68	49	72	22	329	8.6
30-34	26	10	57	54	26	41	18	232	6.1
35-39	12	8	25	20	13	16	10	104	2.7
40-44	5	2	9	8	6	8	4	42	1.1
45-49	1	—	8	3	4	3	2	21	0.6
>50	5	1	3	4	1	2	—	16	0.4
Not stated	1	1	—	—	1	2	4	9	0.2
Totals	379	250	938	735	744	567	206	3819	100.0

about 35 per cent of all cases in recent years. In 1955 this group represented 32.6 per cent of the cases. The vaccine among these children. This is in part borne out by the experience in the 1949 outbreak, when the

TABLE 2. *Bulbar, Paralytic and Nonparalytic Cases According to Age and Sex (Massachusetts, 1955).**

AGE	BULBAR CASES		PARALYTIC CASES		NONPARALYTIC CASES		TOTALS		GRAND TOTALS
	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	
yr.									
0-4	93	58	381	269	209	113	683	440	1123
5-9	119	77	207	142	243	148	569	367	936
10-14	52	39	86	61	90	74	228	174	402
15-19	28	10	55	49	65	26	148	85	233
20-24	14	16	40	57	37	62	91	135	226
25-29	23	28	67	68	49	72	139	168	307
30-34	26	10	57	54	26	41	109	105	214
35-39	12	8	25	20	13	16	50	44	94
40-44	5	2	9	8	6	8	20	18	38
45-49	1	—	8	3	4	3	13	6	19
>50	5	1	3	4	1	2	9	7	16
Totals	378	249	938	735	743	565	2059	1549	3608

*3608 of 3819 cases reported July 1 through November 30 that had been classified.

group twenty-five to twenty-nine years of age was hardest hit, 8.6 per cent of all cases occurring in this age group. It will be seen that the rise among those under five was compensated for by a drop of about 8 per cent in the group ten to fourteen years of age and of only about 3 per cent in those fifteen and over.

The usual preponderance of cases of poliomyelitis among males was seen in this outbreak. Although males constitute only 48.3 per cent of the total population, 57.0 per cent of the cases were among males. The difference was most striking in the group under twenty years of age, in which 60.4 per cent of the cases occurred among males; this cannot be explained by the sex distribution of the population, since males represent only 50.7 per cent of the total under twenty years of age.

Over twenty years of age cases are more numerous among females, only 47.2 per cent of the cases at this age being among males. Here, the difference is largely due to the preponderance of females, males representing only 47.4 per cent of the population over twenty years of age.

The preponderance of cases in males is limited largely to the bulbar and paralytic cases, the sex difference among nonparalytic cases being insignificant.

The figures from which these percentages were calculated are shown in Table 2.

The attack rate by age in 1955 is shown in Table 3. Rates by single years are given for the first ten years of life, followed by attack rates by five-year age groups. Figures for the epidemic year 1949 and for the five-year period 1950-54 are shown for comparison.

The highest rate occurred at five years (318 cases), with rates almost as high at three years (304 cases) and four years (298 cases). The rates for those six, seven, eight and nine years of age were much lower, and at first glance this might be attributed to use of highest rates occurred among the patients six, seven

TABLE 3. *Cases of Poliomyelitis — Age-Specific Case Rates (Massachusetts, 1955).*

AGE	POPULATION*	NO. OF CASES	RATE PER 100,000	1949† RATE PER 100,000	1950-54† RATE PER 100,000
yr.					
<1	97,000	115	118.5	32.0	9.6
1	99,000	197	198.9	70.5	24.6
2	98,000	254	258.2	98.0	24.8
3	96,000	304	316.6	74.4	34.8
4	93,000	298	320.4	119.0	51.7
5	92,493	318	343.8	95.9	61.7
6	91,536	256	279.9	142.0	51.8
7	93,017	135	145.2	132.5	48.4
8	98,688	140	141.9	106.5	48.9
9	82,598	129	156.1	137.0	39.8
(0-4	483,000	1168	242.0	78.2	28.4)
(5-9	458,332	978	213.6	123.2	50.4)
10-14	354,860	427	120.6	120.2	33.0
15-19	312,000	248	79.5	60.0	13.9
20-24	354,000	245	69.3	42.4	11.5
25-29	377,000	329	87.3	40.1	13.8
30-34	361,000	232	64.2	22.2	9.0
35-39	345,000	104	30.2	11.8	4.5
40-44	323,000	42	13.0	40.9	1.7
45-49	296,000	21	7.1	27.4	1.2
>50	1,251,000	16	1.3	.24	1.3
Not stated		9			
Totals	4,915,192	3819	77.5	38.1	12.9

*Numbers in 5-9 age group from school census figures; numbers at other ages estimates, based on birth records & estimated increases in population since 1950.

†Populations used in 1949 and 1950-54 from 1950 census figures.

and nine years old, even though the 1949 epidemic was only half as large as that in 1955.

Geographic Distribution

The distribution of cases by counties shows where the disease was concentrated. The rate per 100,000 population was highest in Plymouth County (167.2) followed by Norfolk (150.4) and Barnstable (148.3). However, the rate in Barnstable County is not realistic because the summer population is more than double the census figures.

Suffolk County (101.8), consisting of Boston and 3 smaller cities, came next, with Middlesex (74.3) and Essex (62.4) following. The 4 western counties, Berkshire (38.1), Franklin (31.6), Hampshire (58.4) and Hampden (22.7), were only slightly involved. Bristol (52.4) and Worcester (52.1) counties were also outside the epidemic area. The rates for Dukes

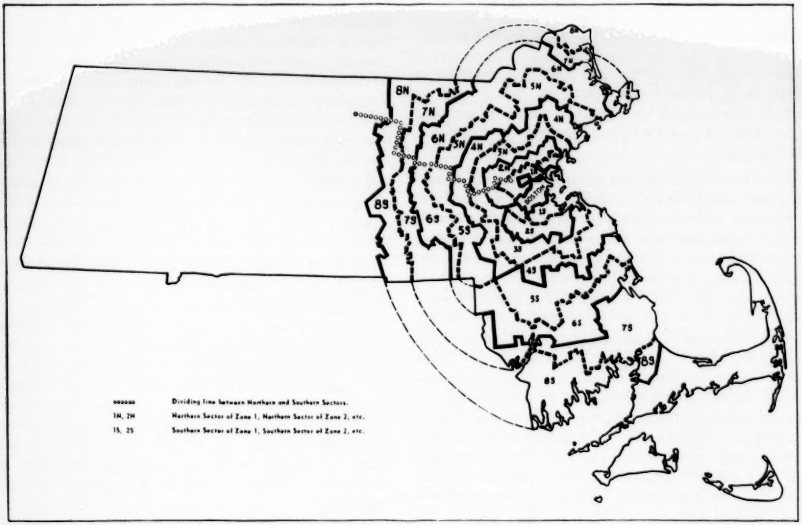

FIGURE 2. *Zones around Boston Used for Calculation of the Weekly Zone Rates of Cases of Poliomyelitis (1955).*

TABLE 4. *Poliomyelitis by Zones around Boston (Rates per 100,000 Population per Week).*

Zone	Population	July				August				September					October				November				December
		8	*15*	*22*	*29*	*5*	*12*	*19*	*26*	*2*	*9*	*16*	*23*	*30*	*7*	*14*	*21*	*28*	*4*	*11*	*18*	*25*	*2*
8-N	42,071	0	0	0	0	0	4.7	2.4	4.7	0	*7.1*	0	0	0	2.4	0	0	0	2.4	0	0	0	0
7-N	50,123	0	0	0	0	2.0	2.0	4.0	*8.0*	0	2.0	0	2.0	6.0	0	0	0	0	0	0	0	0	0
6-N	307,949	0	0	.6	.6	2.9	1.6	3.9	2.6	2.6	*4.2*	1.3	1.6	1.6	1.3	0	.3	.3	0	0	.6	.3	0
5-N	98,797	0	0	2.0	4.1	3.0	5.1	6.1	7.1	8.1	7.1	6.1	4.1	7.1	*11.1*	2.0	5.1	1.0	2.0	3.0	1.0	2.0	0
4-N	153,344	0	.7	4.6	6.5	5.2	10.4	11.7	10.4	9.8	5.9	*18.3*	5.9	8.5	6.5	8.5	5.9	1.9	2.6	1.3	2.6	2.6	0
3-N	171,700	0	1.8	1.2	3.5	8.2	6.4	7.6	*12.3*	6.4	4.7	5.9	3.5	5.3	2.3	4.7	5.3	2.9	5.9	1.2	1.2	1.2	0
2-N	234,210	0	0	2.6	1.7	5.6	5.6	5.1	3.8	3.8	*9.0*	5.1	6.8	3.0	6.4	3.8	2.1	3.0	1.3	.4	1.3	.4	0
1-N	401,573	.5	.5	2.7	1.7	4.7	6.0	7.0	4.5	4.5	4.2	3.5	3.5	3.5	4.0	.8	3.5	3.2	1.7	1.0	1.0	.8	0
Boston	801,444	1.9	4.4	6.6	10.1	10.5	*14.4*	12.6	8.7	7.1	6.9	5.1	3.9	3.0	1.4	0.9	1.5	1.6	1.1	.6	.1	.1	.2
1-S	264,300	.4	.8	3.8	6.0	11.7	*20.8*	15.1	14.0	9.5	6.4	6.8	5.3	3.0	4.2	2.7	4.5	1.9	1.0	.8	1.5	.4	.4
2-S	132,633	.8	2.3	10.6	16.7	27.2	24.2	*34.8*	22.0	12.9	9.1	15.9	8.3	8.3	8.3	6.1	6.1	9.1	3.0	1.5	1.5	1.5	.8
3-S	80,110	0	0	5.0	5.0	17.5	17.5	18.7	*19.9*	18.7	13.7	7.5	7.5	0	3.8	3.8	2.5	1.2	1.2	0	3.8	2.5	0
4-S	143,402	0	0	4.9	8.4	15.4	21.0	*30.7*	16.8	13.9	13.3	7.7	6.3	7.0	6.3	2.1	2.1	1.4	4.9	2.1	0	0.7	0
5-S	127,650	.8	0	3.9	7.9	14.1	*18.0*	10.2	9.4	8.6	9.4	8.6	1.6	3.9	0	6.3	1.6	1.6	1.6	1.6	5.5	0	.8
6-S	97,441	0	2.1	2.1	2.1	6.2	13.3	22.6	9.2	21.6	*24.6*	17.5	5.1	4.1	3.1	9.2	7.2	4.1	1.0	0	3.1	2.1	2.1
7-S	71,171	2.8	0	1.4	9.8	4.2	15.4	7.0	11.2	11.2	12.6	*18.3*	5.6	2.8	2.8	7.0	1.4	2.8	0	0	1.4	0	0
8-S	510,026	.2	0	1.2	.8	2.4	2.4	3.3	2.2	*3.9*	3.1	3.1	2.6	1.6	1.8	2.4	1.6	1.0	.4	.8	.6	.8	.8

(88.8) and Nantucket (85.5) were unrealistic because the population in both is small but was expanded during the summer season by thousands of vacationists. The rate for the State as a whole was 79.4.

Association of Poliomyelitis with Salk Vaccine

Statements have been made that the poliomyelitis epidemic in Massachusetts this year was set off by live virus in the Salk vaccine, but to date no convincing evidence has been brought forward to substantiate this claim.

If the vaccine had started the epidemic, there should have been multiple foci, and the disease should have broken out simultaneously all over the State. Actually, the disease started in Boston and spread in a wave in all directions, but in greater intensity toward the south. To demonstrate this wave, 8 zones around Boston were marked off (Fig. 2). Each zone consisted of a single line of cities and towns outside and immediately contiguous to the previous zone. Each zone made a complete circle of Boston from North Shore to South Shore. A line was drawn toward the northwest through an area of low prevalence to separate the zones into northern and southern sectors. All the cases in the communities in each sector of each zone were totaled for each week, and rates per 100,000 population were calculated. The populations of each sector and the weekly rates are shown in Table 4.

It will be seen that, with two exceptions, the peak of incidence occurred after that of Boston and that the wave started later and persisted longer the farther the zone was from Boston until the eighth zone was reached. The rates in the southern sectors were higher than those in the northern sectors.

There is also evidence that the vaccine did not initiate the disease in Boston itself. The Boston Health Department has advised us that the public poliomyelitis-vaccination program in that city included children in the first and second grades of the public and parochial schools. The single inoculation used was given during the week of May 23-27. Acceptance of vaccination was on a voluntary basis. One lot of vaccine was used for the entire city.

During the six weeks following the completion of inoculations in Boston, 28 cases of poliomyelitis were reported by the Boston Health Department. Of these, in only 2, whose onsets were June 16 and July 5, had Salk vaccine been given. In neither of these patients was the primary paralysis in the limb in which the vaccine was given. That is probably no more cases in vaccinated children than might be expected by chance in a population the size of Boston's. If the vaccination had been responsible for initiation of the explosive outbreak that followed, a substantial number of cases of poliomyelitis would have been expected in the first two weeks after inoculation, as in Idaho, where the outbreak was shown to be due to infectious vaccine.

Perhaps the most convincing evidence that the Salk vaccine did not give rise to poliomyelitis in Massachusetts children who received it in 1955 comes from a substantial group of communities where no cases of poliomyelitis occurred in the first two months of the epidemic. Of the 351 cities and towns in the Commonwealth, 157, all of which participated in the vaccination program, reported no cases before September 1, more than three months after the vaccine was administered.

These towns are distributed in 13 of the 14 counties of the State. The total population of the communities is 389,726, and 13,439 children were given vaccine. If the lots used in Massachusetts contained virus in an infectious state, some cases should have occurred in the children vaccinated in these towns or in their household contacts.

Only three lots of poliomyelitis vaccine, all from one manufacturer, came into the State for use in first-grade and second-grade children. One of these lots consisted of 18,719 9-ml. vials. It was the only lot used in Boston, and it also went into every part of the State. If this lot started the epidemic in Boston, it should have started foci in all parts of the State. It should also have set off an epidemic in Minnesota, since 9708 vials of the same lot went to that state.

The other two lots were small. Massachusetts received 1984 vials of one, and 11,156 vials went to New York State. Massachusetts received 2946 vials of the third lot, and 29,724 vials went to Buffalo, Rochester, White Plains, New York City and other places in New York State. There is no indication that any of the three lots started foci in the other states.

On account of the occurrence of groups of cases of poliomyelitis in certain communities, often involving related families, some of these cases have been cited as evidence of infection by the vaccine or transmissions of poliomyelitis by vaccinated persons. Suggestions have been made that there have been an undue number of cases in household contacts of vaccinated children. In each case investigation has failed to substantiate the rumor.

Effectiveness of Poliomyelitis Vaccine in 1955 Epidemic

When it became apparent that there would be almost as many cases of poliomyelitis in Massachusetts in 1955 as occurred in all the field-trial areas in 1954, the National Foundation for Infantile Paralysis proposed that a special study of the effectiveness of poliomyelitis vaccine be made in the State. A meeting was held on August 24, including representatives of

the Department and the Foundation and several consultants, to plan the study. Funds were provided by the Foundation immediately to employ the necessary office, field and laboratory personnel to carry out the study.

Plan of Study

The main objective of the Massachusetts poliomyelitis-vaccination study was to measure the protection conferred by one or more injections of Salk vaccine in children five to nine years of age.

The study was limited to the children who were vaccinated in public clinics in 1954 and 1955. Practically no children received vaccination privately until late in September, when the epidemic was rapidly waning.

In 1954, over 13,517 children received one, two or three doses of vaccine between May 10 and June 30. In 1955, 4658 of these received a booster dose. The numbers in each age, adjusted to October, 1955, are shown in Table 5. About 14,000 received placebos in 1954. Most of these received vaccine in 1955, a large number receiving two doses. The inoculations in 1954 were limited to the 25 eligible communities that had elected to participate. Inoculations were given to children in the first, second and third grades.

In 1955, 137,892 children received one dose of vaccine, and 9156 two doses of vaccine, between May and June 10, except for a small number who were inoculated after that date, mostly those receiving second doses. The numbers in each age, adjusted to October 1, are shown in Table 5. No vaccine was used in ten communities, which declined to accept vaccine for their first-grade and second-grade children. In the 25 field-trial communities, children in the first, second, third and fourth grades were eligible. In the other communities, only those in the first and second grades were eligible.

There were no inoculated controls in 1955. The study is therefore limited to the observed controls in the ages of those who received vaccine. The control groups are estimated by subtraction of the number of children vaccinated at each single year of life from the total number in that age.

The populations at each age were obtained from the school census of October 1, 1955, from each of the 351 cities and towns.

Reports of cases of poliomyelitis were obtained from physicians and from hospitals under the requirements of the State laws for communicable-disease control. Individual epidemiologic case records for all cases were transcribed by field investigators of the study from the hospital case histories, or from the records of the family physician in unhospitalized cases, on a special clinical and epidemiologic form. The fact that over 90 per cent of all patients with poliomyelitis were hospitalized greatly facilitated obtaining complete information.

So far as possible, stool specimens were obtained from vaccinated patients and from those with nonparalytic cases for virus isolation. Blood specimens were taken from patients with nonparalytic cases in the acute stage when possible, with convalescent bloods two or three weeks later. Laboratory studies were seriously limited by the fact that the study was not undertaken until about two weeks after the peak of the epidemic was reached. Even then it was necessary to obtain additional personnel and equipment for the virology laboratory of the Department of Public Health to meet the greatly increased load. Virus isolations and antibody titrations were carried out in the Virus Laboratory of the Massachusetts Department of Public Health and, for patients hospitalized in the Children's Medical Center, in the Virus Laboratory of that institution under the direction of Dr. John F. Enders and Dr. Sidney Kibrick.

On the basis of experience in the 1954 field survey, it was decided that expert examinations of the patient's muscular status fifty to seventy days after onset of the disease is the best measure of the presence and the extent of paralysis. To ensure accuracy and uniformity of muscle evaluation, only members of the American Physical Therapy Association were employed for the muscle testing. The findings were recorded on the form used in the 1954 field trials. In the larger hospitals employing qualified physical therapists, the muscle examinations were made by

TABLE 5. *Children in Study Population by Age and Vaccination Status (Massachusetts, 1955).*

AGE*	TOTAL POPULATION	CHILDREN RECEIVING NO VACCINE	CHILDREN RECEIVING 1 DOSE IN 1955	CHILDREN RECEIVING 1 DOSE IN 1954	CHILDREN RECEIVING 2 DOSES IN 1955	CHILDREN RECEIVING 2 DOSES IN 1954	CHILDREN RECEIVING 3 DOSES IN 1954	CHILDREN RECEIVING 4 DOSES IN 1954 & 1955	TOTAL CHILDREN RECEIVING VACCINE
yr.									
6	91,536	71,780	19,526	—	224	—	3	3	19,756
7	93,017	35,570	54,711	11	1,230	16	952	527	57,447
8	98,688	45,170	45,122	30	3,181	50	3,338	1,797	53,518
9	82,598	61,428	14,137	27	2,871	48	2,651	1,436	21,170
10	73,258	64,584	4,396	8	1,650	9	1,716	895	8,674
Totals	439,097	278,532	137,892	76	9,156	123	8,660	4,658	160,565

*As of Oct. 1, 1955.

such therapists. In Boston the physical therapists of the Visiting Nurse Association made the tests under contract. In other areas the examinations were made by therapists employed by the study or by those of the staff of the Crippled Children's Services of the Massachusetts Department of Public Health. All physical therapists who participated in the study were given prior orientation in the abridged method of muscle grading of the D. T. Watson School of Physiatrics.

Muscle evaluations were obtained for all but 48 of the cases in the study. In most of these, onset had occurred less than fifty days before drafting of the report.

TABLE 6. *Secondary Cases of Poliomyelitis among Vaccinated and Unvaccinated Children Exposed to a Primary Case in the Household (Boston, 1955).**

AGE	SALK VACCINE, 1 DOSE		NOT VACCINATED		RATE
	NO. EXPOSED	SECONDARY CASES	NO. EXPOSED	SECONDARY CASES	
yr.					%
0- 4	4	0	506	12	2.4
5- 9	139	0	211	7	3.3
10-14	1	0	172	4	2.3
Totals (0-14)	144	0	889	23	
Average					2.6

*Unpublished data by courtesy of Wheeler & Foley.[3]

Final diagnosis of cases and the type and severity of poliomyelitis was based on the history and clinical findings and the fifty-to-seventy-day muscle evaluations, supplemented by laboratory data when available. Decision in individual cases was made without information of the vaccinal status so far as possible.

To assist in the interpretation of the data collected in the study and to provide professional guidance in their respective fields, the following consultants provided their services: Dr. William T. Green (orthopedics); Dr. R. Cannon Eley (pediatrics); Dr. John F. Enders (virology); Dr. Hugo Muench (vital statistics); and Dr. Robert F. Korns (epidemiology).

Fatal Cases

Among the children six to ten years of age, 21 deaths were ascribed to poliomyelitis up to November 1, 1955. This gives a mortality of 3 per cent for the entire group. Of these 21 deaths, 1 occurred in a child who had received one injection of Salk vaccine in May, 1955. The cause of death was confirmed by autopsy. All fatal cases in the age group studied were checked individually with the records of the hospitals in which death took place. In only 7 cases was permission for autopsy obtained. In these, postmortem findings confirmed the diagnosis of poliomyelitis. All local boards of health in the State were circularized at the end of the study to ensure complete reporting of deaths from poliomyelitis in the group six to ten years of age in their respective communities.

Boston Study

Some measure of the protection apparently conferred by a single inoculation of Salk vaccine is provided by a study by Wheeler and Foley,[1] of the Boston Health Department. Among 144 vaccinated children exposed to a primary case of poliomyelitis in the family, no secondary cases occurred. In a group of 889 unvaccinated children similarly exposed, poliomyelitis developed in 23, or 2.6 per cent (Table 6).

TABLE 7. *Cases of Poliomyelitis in Study Population (Rates by Vaccination Status).*

TYPE OF ATTACK	PATIENTS NOT VACCINATED	RATE*	PATIENTS RECEIVING 1 DOSE	RATE*	PATIENTS RECEIVING 2 DOSES	RATE*	PATIENTS RECEIVING 3 DOSES	RATE*	PATIENTS RECEIVING 4 DOSES	RATE*	TOTAL CASES
Paralytic	437	157	87	63	5	55	4	46	1	21	534
Nonparalytic	116	42	43	31	1	11	2	23	2	42	164
Totals	553		130		6		6		3		698

*Rates per 100,000 population, using as denominators number of children receiving specified number of doses of vaccine.

The criteria for classification of cases of poliomyelitis outlined in the summary report of the 1954 field trials and the definition of "paralytic" and "nonparalytic" cases were utilized in this study. Bulbar, bulbospinal and spinal cases were combined to form the total paralytic group. The grades of spinal paralysis were determined by the scores of the muscle evaluation. The degree of bulbar paralysis was indicated by the extent and severity of involvement.

The final diagnosis in each case was reviewed by one member of the medical staff, after full consideration of the clinical findings, muscle evaluation and laboratory data.

Evaluation of Results

The distribution of the children in the study population is shown in Table 5. Out of the 439,097 children in the ages six through ten, a total of 160,565 had received one or more doses of poliomyelitis vaccine. Only 2082 children in other ages received vaccine of the public program. Most of the vaccinated children, therefore, were in the study population.

The only group in which significant rates can be calculated is that receiving only one dose of vaccine. Only 22,673 children received two or more doses of vaccine, and these are distributed among three groups.

The distribution of the 698 cases used in the evaluation is shown in Table 7. Of these, 130 occurred among the children who received one dose of vaccine, and only 15 among those who received two or more doses. The rate per 100,000 among the nonvaccinated children was 157, that among those receiving one dose was 63 for those with paralytic poliomyelitis, and the rates among those receiving two or more doses were slightly less. The rates among the nonparalytic cases showed much less difference.

Attack rates among the vaccinated and unvaccinated were much higher than those in the Francis report[2] on the field trials of 1954. In the areas where controls received placebos, the attack rate of paralytic poliomyelitis among vaccinated children was 16 per 100,000, and the rate among controls was 57. In the observed areas the paralytic-attack rate among the vaccinated was 17 per 100,000, and the rate among the controls was 46. As noted above, comparable figures in Massachusetts in 1955 were 63 per 100,000 among the vaccinated who received only one dose and 157 among the unvaccinated. This difference in attack rate is due to the fact that the general incidence in the 1954 study areas was low, whereas the incidence was unusually high in Massachusetts in 1955.

TABLE 8. *Estimates of Effectiveness of Poliomyelitis Vaccine.*

TYPE OF CASE	NO. OF CASES OF POLIOMYELITIS			ESTIMATE OF EFFECTIVENESS	
	CHILDREN NOT VACCINATED	ONE DOSE OF VACCINE	TWO DOSES OR MORE	ONE DOSE	TWO DOSES OR MORE
				%	%
All cases	553	130	15	53	67
All paralytic	437	87	11	60	69
Bulbospinal	124	21	4	66	60
Bulbar	63	11	1	65	80

It is necessary, therefore, to make estimates of effectiveness to compare our figures with those of Francis (Table 8). Estimates of effectiveness were calculated only for Type 1 poliomyelitis because there were almost no cases due to the two other types among those on whom virus isolations were attempted. It will be noted that the effectiveness among those who received one dose for all cases, including the nonparalytic, was 53 per cent. In the report of Francis et al.[2] the vaccine was 62 per cent effective in observed areas and 68 per cent in the placebo areas. The fact that one dose approached so closely the value of three doses, particularly in an epidemic situation, suggests that the vaccine used in Massachusetts in 1955 was a particularly effective one. This is in part confirmed by titration done by Salk (Fig. 3) on the three lots used. The best lot was the largest one.

The effectiveness for two or more doses is even higher, but since this figure is based upon only 15 cases, no conclusions should be drawn.

This is a preliminary report on the 1955 experience in Massachusetts. Another paper will deal with information collected during the next few weeks and with figures that could not be analyzed for this paper.

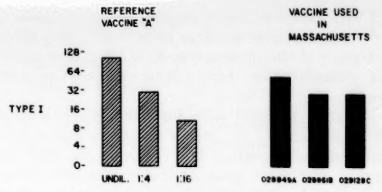

FIGURE 3. *Geometric Mean Titer of Antibody Induced in Groups of 12 Monkeys.*

Three lots of vaccine used in Massachusetts are compared with three different dilutions of reference vaccine A.

SUMMARY

An unprecedented epidemic of poliomyelitis in Massachusetts in 1955 provided an excellent opportunity to evaluate the effectiveness of poliomyelitis vaccine in an epidemic situation.

The main characteristics of the 1955 epidemic are described. The epidemic was due almost exclusively to Type 1 virus.

The possibility that live virus in the vaccine used in May and June initiated the epidemic is discussed.

A total of 130 cases occurred among the 137,968 children who received one dose of vaccine, an attack rate of 94.5 per 100,000. Fifteen cases occurred among the 22,673 who received two or more doses, a rate of 66.4. The rate among the 278,532 unvaccinated children (553 cases) was 198.2 per 100,000.

The effectiveness of the vaccine for all cases of poliomyelitis was 53 per cent. For paralytic cases only the effectiveness was 60 per cent. These figures parallel those of Francis and his associates for protection against Type 1 poliomyelitis.

We are indebted to Mrs. Joan Daniels, of the Virology Laboratory of the Massachusetts Department of Public Health, to Dr. Sidney Kibrick, of the laboratory of the Children's Medical Center, for the virus and serologic data used in this study, and to Mrs. Margaret Sandin, chief physical therapist, who supervised the muscle evaluations.

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MEDICAL PROGRESS

OTOLOGY — ACUTE MIDDLE-EAR DISEASE

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THIS progress report emphasizes the growing interest in acute secretory otitis media, with special reference to the preservation of hearing, and clarifies its differentiation from acute suppurative otitis media.

In 1869 Politzer[1] gave his first clear description of acute secretory or, as it is sometimes called, acute catarrhal otitis media. The condition has been well known ever since then, and textbooks have clearly defined and differentiated this disease from acute suppurative otitis media. However, only a few studies were made in this country until 1940. This date coincided with a growing awareness that acute secretory otitis media was on the increase. The problem became more challenging as more accurate audiometric methods of estimating hearing loss were made available not only for individual patients but also for large groups such as school children who could be tested en masse and screened and then referred for special study if found to be deaf. Studies in the fields of allergy, fluid chemistry and climatology and even a restudy of anatomy of the eustachian tube were undertaken to clarify the etiology and pathogenesis.

Before discussing these points, I should like to recapitulate the textbook picture of this condition. Acute secretory otitis media is the result of eustachian-tube obstruction. It is a sterile condition as contrasted with suppurative otitis media, in which the middle-ear cavity is infected. Owing to the development of vacuum by absorption of air in the blocked middle-ear cavity, the drum is retracted, and there is often a transudation of fluid into the cavity to take the place of the rarefied air. This fluid is either serous or mucoid in character.

SYMPTOMS

The most common symptom is deafness. This is usually acute in onset, variously described by the patient as a "full feeling" or a sensation of a "head in a barrel" or "water in the ear." Occasionally, if the middle ear is only partly filled with serum, the deafness will change with the position of the head. A strange hyperesthesia is sometimes noted when the auricle on the same side is touched. Pain and tinnitus may occur but are not constant findings. The pain, if present, is not usually as severe as that of acute suppurative otitis media. Since this condition is secondary to nasal or nasopharyngeal lesions, the symptoms of the associated disease are present. Fever and hematologic changes, if present, are due to these latter conditions rather than to the otitis media.

DIAGNOSIS

In the earliest stage, the drum is retracted. At first the color may be more or less red, owing to engorged blood vessels in the middle ear rather than to infection, for the middle ear is sterile. Because the predominant factor is the tubal closure, with resulting middle-ear negative pressure, fluid transudate may now appear. This is either serous or mucous (not purulent). The color becomes more yellowish, and often a meniscus may be observed if the middle ear is not completely full of fluid. Davison[2] stresses the information to be obtained by the use of a pneumatic otoscope:

> The most important single diagnostic method which in my opinion is almost invaluable is the use of the pneumatic otoscope. If there is fluid in the middle ear, the drum moves poorly. The degree of impairment of mobility is in proportion to the amount of fluid in the middle ear. If the drum flutters rapidly in response to rapid alteration in air pressure produced by the hand bulb, one can be certain that there is little or no fluid in the middle ear.

In testing the degree of deafness by means of the audiometer, one finds that the curve is usually flat — that is, there is uniform loss for all frequencies. However, Löwy[3] and others have noted that in about a third of all cases loss in the higher tones is especially marked: a condition usually associated with inner-ear disease but attributed by Löwy to impaired mobility at the round window due to increased middle-ear tension.

ETIOLOGY

A number of theories have been advanced to explain the apparent increase in incidence of this condition. Hoople[4] considers that physicians are more on the lookout for this condition. In my own experience this is true, but also the patients seem to be coming in ever-increasing numbers and since doctors have always been aware of the clinical picture I doubt whether it has really been missed very often. It seems to me, therefore, that there is an actual increase in the number of cases. Eagle[5] suggests that viral infections in the middle ear may account for some of this, but until diagnostic methods are more widely available to determine the presence of a virus, this point is still debatable. Also, one sees hypovirulent infections owing to increasing use of antibiotics and

chemotherapy, which check the infections to a certain extent but without relieving the fluid trapped by the obstruction in the eustachian tube. Therefore, what originally was a bacterial disease in the nasopharynx and eustachian tube ends up as a sterile otitis. Also, a condition called aero-otitis, which is due to the blocking of the eustachian tube and change of atmospheric pressure caused by sudden loss of altitude in airplane flights, results in negative air pressure in the middle ear and a transudation of fluid into that cavity.

Suehs[6] studied 372 patients with acute, subacute, and chronic serous otitis and gives the causes listed in Table 1.

TABLE 1. *Etiology in 372 Cases.*

ETIOLOGY	ACUTE CASES	SUBACUTE CASES	CHRONIC CASES	TOTALS
Acute upper respiratory infection	111	35	16	162
Sinusitis	24	16	19	59
Hypertrophied adenoids (without apparent allergy)	7	20	37	64
Allergy	19	7	11	37
Previous suppurative otitis media only cause	0	0	3	3
Aero-otitis	9	1	0	10
Contagious disease (measles, mumps)	2	0	0	2
Pregnancy (endocrine)	1	0	0	1
Hodgkin's disease	0	0	1	1
Malocclusion	0	2	3	5
Cancer of nasopharynx	0	0	2	2
Swimming	3	0	0	3
Unknown	7	9	7	23
Totals	183	90	99	372

It will be seen from this study that although acute infections account for the greatest number of cases in the acute group, adenoids and other structural factors are more often the cause in the chronic group. A hundred and twenty of these patients were under ten years of age. Suehs[6] also conducted a nation-wide survey to determine what effect, if any, climate might have on the incidence. The results, on the basis of observation of 20 widely distributed otologists, were that a patient with pre-existing disease in the eustachian tube is more likely to have tubal obstruction with effusion in a moist climate at or near sea level than he would in a high dry climate.

Allergy seems not to play as large a part as one would expect. Only 37 (10 per cent) patients gave this as a cause, and a search for eosinophils in the exudate from the ear proved fruitless.

Regarding the chemistry of the fluid, many observers have had widely varying findings. Some found low protein in the serous and high protein in the mucoid type, and others vice versa. More accurate methods of collecting may be necessary and many more observations must be made.

In a study of 100 cases Davison[2] gave a clear analysis of the salient factors in etiology and the pathology of the fluid (Tables 2-6).

TABLE 2. *Etiologic Factors in 100 Cases.*

FACTOR*	NO. OF CASES
Acute upper respiratory infection	53
Large adenoids	44
Chronic sinusitis	4
Obesity	4
Hypothyroidism	2
Tumor of nasopharynx	1
Vasospasm due to nervous tension	2

*Sometimes, 2 or more factors present in same case.

THERAPY

In all cases in which fluid is obvious or even suspected in the middle ear, if improvement is not obtained by relief of the obstructed eustachian tube and inflation of the middle ear by means of a Politzer bag or catheterization, it has been generally recommended that a myringotomy be performed. This is especially true when the fluid is mucoid, for it is then so tenacious that it is most difficult to evacuate unless one can use direct suction at the myringotomy incision. Even then inflation of the middle ear combined with suction may be necessary. This procedure in doubtful

TABLE 3. *Etiology of Tubal Obstructions.*

ORDER OF IMPORTANCE	CAUSE
1	Inflammatory edema of tubal mucosa
2	Allergic edema, including bacterial allergy
3	Large adenoid
4	Infected lymphoid tissue in nasopharynx
5	Cysts or tumors in nasopharynx
6	Obesity
7	Hypothyroidism

TABLE 4. *Adenoid Factor in 100 Cases.*

FACTOR	NO. OF CASES
Large adenoid combined with allergic constitution	23
Large adenoid without allergic constitution	21
Total	44

TABLE 5. *Type of Fluid in 100 Cases.*

TYPE OF FLUID	NO. OF CASES
Thin serum — often amber in color	51
Mucus — often extremely thick & viscid	49
Serum in one ear & mucus in other ear*	4

*Sometimes, serum with 1 attack & mucus with next.

cases is of some diagnostic importance. If no fluid is found, no harm has been done either. In fact the middle ear will clear up sooner with the restoration of normal air pressure, and the drum is usually healed in twenty-four hours.

TABLE 6. *Type of Fluid According to Patient's Constitution.*

CONSTITUTION & FLUID	NO. OF CASES
Nonallergic constitution	54
Mucus	21
Serum	33
Allergic constitution	46
Mucus	28
Serum	18

In some very resistant cases of chronic mucoid otitis, it has been necessary to perform a mastoidectomy, a seemingly radical procedure but in such cases the one of choice as the secretory process had extended from the middle ear into the adjoining mastoid cells.

Davison,[2] in commenting on the treatment in his series, pointed out that all his patients responded well under this regimen although he does not advocate catheterization, since he fears irritation and trauma to the eustachian orifice. It is also noteworthy that 58 per cent of the patients in his series were under ten years of age. Recurrences were more common, as one would expect, in those with large adenoids and in those with recurrent nasopharyngitis. As the symptoms of the nasopharyngeal disease subside, he stresses the importance of examination for residual secretory otitis media. Children five years of age and over can usually co-operate quite well and can be given an audiometric test with some accuracy.

The use of radium and x-rays for the enlarged adenoid is still not generally adopted. Surgical removal under direct view, as advocated by Meltzer,[7] seems to be a surer method of coping with this situation. Obviously, when the condition is acute because of sinusitis or nasopharyngitis with tubal infection, proper chemotherapeutic or antibiotic treatment is indicated; it is also quite obvious that the removal of intranasal obstruction, whether it is due to deviated septum, hypertrophic turbinates, nasal or choanal polyps, is essential in the prevention of recurrent attacks. Moreover, specific treatment with the drugs is for the purpose of clearing up the primary condition in the nose and nasopharynx rather than directed to the middle ear, which in these cases is not infected.

ACUTE SUPPURATIVE OTITIS MEDIA

This disease is differentiated from the secretory type on the basis of the pathological as well as the clinical picture. The essential difference is that the suppurative type is due to bacterial invasion in the middle ear. It may be mild and subside spontaneously in a few days or may rapidly develop to the suppurative stage, with a bulging red drum, severe pain and headache and an accompanying rise in temperature and leukocyte count. Early mastoid tenderness is sometimes present, but usually subsides as soon as drainage has been obtained by myringotomy. This primary tenderness, of course, is not to be confused with late tenderness, which indicates periostitis caused by extension of the inflammatory process through the cortex.

I have recapitulated these findings because the points of diagnosis are not too well known to the recent graduates of medical schools, the reason being the obvious one of a marked change in the teaching material because of the newer drugs. Many students have never seen an operable mastoid and so are not now on the alert when they have to deal with an acute condition of the ear.

Since the introduction of chemotherapeutic drugs and the discovery of the antibiotic agents, probably few fields of medicine have been as profoundly affected as that of otolaryngology. This was especially true when penicillin first made its appearance. So dramatic was the change in the clinical picture of otitis media and its mastoid complications that in some hospitals not only did mastoiditis vanish from the picture but also the severity of acute suppurative otitis media had been so checked that often even a short course of a drug would clear up the symptoms. Whereas formerly an acutely inflamed, bulging drum was almost always opened surgically, or broke spontaneously, with the drug the signs and symptoms receded so rapidly that the thought that antibiotics had replaced the paracentesis knife became widespread, and seemed to have considerable justification. It also seemed to some that, for practicable therapeusis, it was only of academic interest to differentiate the acute suppurative from the secretory or catarrhal type of acute otitis media.

Of late the picture of acute middle-ear infection is less clear because of certain new factors related to bacteriologic response to the drugs. It seems the pendulum has begun to swing slightly back toward the prechemotherapeutic days. Perhaps one should have anticipated this as a typical biologic response. In time, all life makes an adjustment to its changing environment or becomes extinct. For instance, organisms formerly very sensitive to antibiotics have begun to become resistant, especially hemolytic *Staphylococcus aureus*. A greater number of gram-negative organisms as well as *Proteus vulgaris* and *Pseudomonas aeruginosa* are being cultured from middle-ear discharge, and these organisms have never responded particularly well to any antibiotic. Patients frequently show allergic reactions to antibiotics and for that reason are unable to obtain help

from them when acute otitis media develops. Also, inadequate dosage with the proper drug or the use of an improper drug or failure to recognize residual infection, which flares up again with progression of disease when the drug is withdrawn, and temporizing with the infection in the face of nonresponse to the drugs are undoubtedly significant factors in the failure to obtain a successful result.

Whereas all authors are in agreement about the marked drop in surgical mastoiditis that followed the introduction of the sulfonamides, and then the general use of penicillin about 1946, statistical reports have varied widely, quite possibly because such variations occurred from year to year and from place to place in the days before any of the drugs were used. For this reason the higher incidence of mastoiditis in the prechemotherapeutic days in some clinics may be explained by the fact that the infection involved an organism whose virulence had been stepped up, and it is hard to evaluate the response to these drugs in these later years, for the method of administration and the indication for which the drug is given may vary considerably. Generally speaking, the method most in favor at present is well illustrated by Davison,[8] who states that because organisms are becoming resistant to the low doses previously used, much larger doses should be given and over a much longer period. He particularly disapproves of the administration of one injection of penicillin followed by penicillin by mouth for three or four days. In his clinic he gives children up to 3,000,000 units of procaine penicillin daily for those under six years of age, and 5,000,000 units for those over six years of age, and gives adults up to 10,000,000 units daily. These seem like very large doses, but his results are imposing. In 1937 he had patients with otitis media with mastoiditis, of whom 58.9 per cent came to surgery. Since 1946, to maintain a low rate of surgery, he has had to resort to larger and larger doses (Table 7).

Regarding myringotomy in acute suppurative otitis media, Davison[8] makes the following statement:

> It should be realized that acute otitis media and acute mastoiditis are not separate aand distinct processes. There is some degree of mastoiditis with every otitis media which has persisted for more than three or four days. If this mental picture was firmly planted in the minds of all physicians treating otitis media, I think there would be less tendency to delay early myringotomy and early administration of one of the antibiotics.

He quotes Rutherford[9] as follows:

> The complacent acceptance of the antibiotics as a cureall in acute otitis media has led to a state where the younger pediatricians do not know the art of cleansing the ear canal: of observing and recognizing the changes in the tympanic membrane which indicate pathological conditions in the middle ear; or how to do a myringotomy. In fact some have been taught that myringotomy is not only an unnecessary procedure but one to be avoided because it injures and scars the tympanic membrane, although spontaneous rupture of the drum under antibiotic therapy apparently is not considered harmful. They do not differentiate between suppurative and nonsuppurative otitis media.

Rutherford[9] further states, "natural immunity may not be acquired when drugs are used and the organisms may regain their former activity when the drug is discontinued." Davison's[8] comment on this opinion is as follows:

> It seems pointless to argue whether use of penicillin is superior to use of myringotomy or vice versa. A sensible attitude is to employ both measures as soon as the diagnosis is made. During the last ten years I have not had to perform a mastoidectomy for any patient who came to me for initial treatment of the otitis media . . . [In follow-up treatment] incomplete resolution can be determined if one uses a pneumatic otoscope. Impaired mobility of the drum is an indication for repeated myringotomy and aspiration of the exudate in the middle ear. The so-called masking effect of the antibiotics is no problem for the man who is experienced in the use of these procedures. A normal audiogram is additional evidence of a normal middle ear.

Although he uses in vitro tests for sensitivity, he believes that the really dependable means of assessing the effect of an antibiotic in a given case is the therapeutic response. But if there is no response after forty-eight hours, a sensitivity test is done on the material cultured from the myringotomy. In his cases 76 per cent of children who had otitis media also had enlarged adenoids, and to this fact he attributes the predisposition to the development of otitis media.

TABLE 7. *Decreasing Frequency of "Simple" Mastoid Operations at the Geisinger Hospital.*

YEAR	PERIOD	NO. OF CASES OF ACUTE OTITIS MEDIA & MASTOIDITIS	NO. OF "SIMPLE" MASTOID OPERATIONS	PATIENTS REQUIRING MASTOIDECTOMY
				%
1937	Presulfonamide	202	119	58.9
1943	Sulfonamide	282	74	26.2
1946	Small doses of penicillin	247	10	4.0
1949	Large doses of penicillin	189	5	2.7
1950	(1,000,000 to 3,000,000 units daily)	158	9	5.7
1951	(1,000,000 to 3,000,000 units daily)	109	1	0.9
1952	(1,000,000 to 3,000,000 units daily)	110	3	2.7
1953	Larger doses of penicillin	122	0	0
1954	(5,000,000 to 10,000,000 units daily)	65	2	3.0

Lahikainen,[10] in a careful bacteriologic study of the secretions obtained by myringotomy in 734 ears among 566 patients, found Type 3 pneumococcus in 81, pneumococcus of other types in 201, *Streptococcus pyogenes* in 177, *Str. viridans* in 24, *Haemophilus influenzae* in 112 and no growth in 126 cases. Sensitivity tests showed that all infections due to *H. influenzae* were sensitive to sulfathiazole but not to penicillin. No other organisms that were recovered

showed resistance to penicillin, which was given in 176 cases, with no complications. In 453 cases no antibiotic or sulfonamide was given. Myringotomy alone appeared to be the treatment. In this group there were 9 complications (2 per cent of the total). Seven patients had mastoiditis, 1 had meningitis due to *Str. viridans* and 1 lateral-sinus thrombosis and brain abscess (the only fatal case) due to Type 3 pneumococcus.

In a study based on the experiences of Goodale and Montgomery[11] during the 1954-55 winter service at the Massachusetts Eye and Ear Infirmary, it was apparent that certain errors were current in recent teaching. During the two-month period, 15 cases of acute mastoiditis requiring surgery formed the basis for the conclusion that the chief cause of operation was, first of all, the attitude that acute otitis carries no great implications of danger and that merely arresting the pain and temperature by antibiotics is all that is needed to obtain a cure. (One may call this the attitude of complacency.) A second cause was a reluctance to consider suppurative otitis media a surgical disease. It is quite obvious that in any case of retained pus, drainage is necessary, for, as Fleming[12] has pointed out, the drug must come in contact with the bacteria directly. The presence of undrained purulent secretion frequently prevents just such an occurrence. Also, in the opinion of Goodale and Montgomery,[11] the best bacteriologic determination can be obtained from a culture taken directly from the middle-ear secretions at the time of myringotomy. They stress also the importance of a culture before the administration of penicillin or other antibiotics. If one wishes to give any drug during the interval between the taking of the culture and its report, sulfadiazine, which does not have the effect of inhibiting the growth in vitro, may be given. Finally, it is pointed out that at present many organisms, principally strains of staphylococci, have developed specific resistance to one or more of the antibiotics. Furthermore, organisms such as *Ps. aeruginosa* and *H. influenzae* have appeared in increasing numbers. It seems obvious that bacteriologic studies are essential and that on certain occasions sensitivity tests must be done to select the proper antibiotic.

If these principles are not considered, an increasing number of mastoidectomies may become necessary — a reversal of the trend noted up to the present. One wonders why there seems to be such opposition to a simple myringotomy and such fear of "traumatizing" the drum, with disregard of the real danger from the presence of purulent exudate in the middle ear and of its implications of loss of hearing function, or the possible extension of disease to other regions of the ear.

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MEDICAL INTELLIGENCE

A NOTE ON THE ASSOCIATION OF EMPHYSEMA, PEPTIC ULCER AND SMOKING*

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ALAN L. MICHELSON, M.D.,§ AND
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THE following discussion suggests a relation between emphysema, peptic ulcer and smoking and tentatively places a heavy responsibility on the last in the pathogenesis of the first two. In the course of the past eighteen months, 25 patients with chronic obstructive pulmonary emphysema were studied. These patients were unselected and came under observation only because of the presence of advanced pulmonary disability. A review of the histories in this group revealed that all had been heavy smokers, and with the exception of 1 male patient who stated that he had smoked cigars exclusively, all had smoked cigarettes for twenty years or more. Some had stopped smoking when respiratory symptoms developed. A history of smoking has been consistently found in patients with cough syncope,[1] a not unusual concomitant of pulmonary emphysema.

The group comprised 19 men and 6 women, ranging in age from fifty-one to eighty-one years. All complained of dyspnea of three or more years' standing, and, except for 3 male patients with cardiac disease apparently secondary to their pulmonary lesion (cor pulmonale), none had any recognizable cause for their respiratory symptoms other than the presence of obstructive change in the airway. All had some reduction in the vital capacity and marked slowing of expiration as demonstrated by the expirogram,[2] less than 50 per cent of the vital capacity being exhaled in the first second. The residual volume was 50 per cent or more of the total capacity in all 11 patients in whom this measurement was made. Three patients, all males, in this group had bronchogenic carcinoma. Eighteen patients were treated intensively with steroids, and although symptomatic improvement was clearly induced in 16, none had more than slight or, at best, moderate improvement in lung function as judged by the expirogram or, in some cases, by more elaborate tests of pulmonary function.

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EMPHYSEMA AND BRONCHIAL ASTHMA

Unfortunately, the criteria by which emphysema, as the term is used here, is to be distinguished from bronchial asthma, have never been clearly established. We believe that the distinction can be made in most cases. Asthma usually begins early in life, but irrespective of the age at onset, periods of severe dyspnea — associated with a reduction in maximal expiratory rate — tend to alternate with periods of normal or close to normal exercise tolerance and pulmonary function can be restored in a remarkable manner with intensive steroid therapy. In the progressive and often ultimately fatal form of obstructive pulmonary disease referred to here as emphysema, on the other hand, there is usually no dyspnea or other evidence of functional impairment of the lung before the age of forty, there is a gradual loss of pulmonary reserve, and, although there may be variations in degree once respiratory symptoms have become manifest, there are no complete remissions. Finally, the maximal expiratory rate is markedly reduced, an abnormality that can be at best only partially removed by intensive treatment with bronchodilator drugs or steroids, or both. Whether or not this will be accepted as an adequate characterization of the disease, all patients in the group of 25 mentioned above fulfilled these criteria.

Certain features of emphysema can be explained by the assumption that the disease is an inflammatory lesion of the bronchial tree caused by the inhalation of minute irritating particles. The emphysematous patient with dyspnea and obvious obstruction to expiration often has a remarkably silent chest on auscultation. In contrast, the asthmatic patient with dyspnea usually wheezes audibly. This may be due to a difference in the location of the lesion. In asthma, obstruction may be chiefly in the relatively large noise-producing airways, whereas in emphysema this may be restricted to the terminal portion of the airway.[3] Here, the small caliber of the airway and the low velocity of flow minimize turbulence, the cause of wheezes and rhonchi. Such a distribution of the lesion in the two conditions might arise from a difference in the size of the particles inhaled, those recognized as causes of asthma (pollens, mold spores and dusts) being relatively large and tending therefore to settle out in the larger airways, and those that we believe to cause emphysema (smoke and possibly fumes and certain industrial dusts presumably acting as irritants) being minute and therefore capable of reaching the periphery of the lung.

ASSOCIATION WITH PEPTIC ULCER

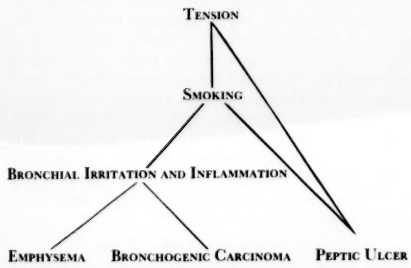
We were further struck by the occurrence of peptic ulcer in 6 of the 25 patients with emphysema referred

to above, a prevalence of 24 per cent. That this was not mere chance is suggested by two published reports emphasizing such a relation. In one series of 70 patients with benign gastric ulcer there were 40 cases of "chronic lung disease" that, though not described in detail, appear to have been in the main what we are calling chronic obstructive emphysema.[4] In another series[5] of 700 consecutive autopsies in males, ulcer was approximately three times as frequent in those with emphysema (19 per cent) as in the group as a whole (6.4 per cent), and the rate of occurrence of ulcer in those with bronchogenic carcinoma (a condition in which an association with cigarette smoking is widely accepted) was 17 per cent. This report also included 72 living patients with "chronic pulmonary disease," of whom 14, or 19 per cent had ulcer.

Discussion

An association appears to exist, therefore, between cigarette smoking and emphysema on the one hand and emphysema and peptic ulcer on the other. We believe that the presence of cigarette smoking in this association is best explained as a cause in emphysema and an aggravating circumstance and possibly a cause in ulcer. Such an assumption explains the following: the finding that all of a group of 25 patients with emphysema were cigarette smokers of long standing; the reported description of the lesion in emphysema[3] as inflammation and obstruction of the peripheral and narrow portion of the airway; the widely held opinion that smoking aggravates peptic ulcer[6]; the frequency of peptic ulcer in patients with emphysema; and the occurrence, in the group of 25 patients with emphysema, of 3 cases of bronchogenic carcinoma, a disease for which an association with cigarette smoking appears to have been established.

The quantity and manner of smoking (inhalation) or both may be influenced significantly by the personality of the subject, which is here regarded as having a direct bearing, therefore, on the development of both emphysema and peptic ulcer. A simple schema representing the interrelations herein postulated is as follows:



"Tension" is loosely used here to represent a constellation of emotional states and habits ordinarily attributed to those who are anxious, frustrated, ambitious and so forth and who, perhaps because of added factors yet to be defined, may be led or pushed to smoke. Relations other than those indicated may also exist — for example, anxiety produced by respiratory difficulty causing or aggravating ulcer.[3]

It is therefore suggested that emphysema and perhaps peptic ulcer as well should be assigned a place along with carcinoma of the lung in the tobacco controversy. Intensive study of this question appears to be warranted since emphysema as defined above is a disease more common than carcinoma of the lung and has a prognosis almost as gloomy.

Since this paper was submitted for publication, our attention has been called to two other studies concerning a relation between smoking and pulmonary emphysema.[7,8]

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THOMAS DE QUINCY AND THE MEDICAL PROFESSION

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In one of Thomas De Quincy's narrative and miscellaneous papers, the *Spanish Nun,* two passages have a certain medical interest. The first evokes one's curiosity by his use of the word *antiseptic* in a sense that suggests to a modern reader the meaning it has derived only since the discoveries of Pasteur, Koch and Lister. Yet De Quincy died in 1859, seventeen years before Pasteur's work on the fermentation of beer and Koch's isolation of the bacillus of anthrax, and still longer before Lister's application of the antiseptic method to surgery. One wonders when the word became current in the English language and what its precise connotation could have been. To De Quincy, at least, it meant *resistant to putrefaction,* about which the effect of extreme heat and extreme cold were known, but without any knowledge of the cause and the nature of the degenerative process. Yet by the casual reader of today the anachronism involved in imputing to De Quincy the present meaning of the word would hardly be noticed.

The heroine of the *Spanish Nun* had escaped from a convent in the guise of a man, a deception so successfully maintained that she was able to join a military expedition to South America, where she covered herself with glory by feats of arms and became a cavalry officer. After a series of incredible adventures she deserted the army, and with two male companions and a horse she set out on a hazardous attempt to cross the Peruvian Andes. Lack of food and the bitter cold of the high altitudes brought the party to the point of exhaustion. They were obliged to kill the horse, hoping to subsist for some days on the meat. They were faced by the question of how to keep the supply of meat from spoiling. "No saltpetre or sugar could be had; but the frost was *antiseptic;* and the horse was preserved in as useful a sense as ever apricots were preserved or strawberries." The meaning was simply "preservative" as applied to food subject to decay. In short, the word was ready-made years before it was taken over and applied to chemical substances capable of destroying or inhibiting the growth of pathogenic micro-organisms. Who, today, could have imagined that the word had any significance other than its current meaning?

The second passage of medical interest is a humorous but, one may guess, seriously meant challenge to the authority of medical experts. In the course of the wanderings of the Spanish nun De Quincy remarks that at moments when she was on the verge of fatal collapse from exhaustion a spoonful of brandy would have ensured her survival (she did survive). This seems to have been a hobby of the author, but he refrains from interrupting the narrative to expatiate on the subject. Instead, he refers the reader, by a footnote, to an appendix, where he gives free rein to his ideas on the common sense of the layman as against the inflexible theories of doctors. Such ideas are doubtless often encountered by the practicing physician today though with less excuse than could be found a hundred years ago, when medical authority tended to be more dogmatic on its empirical basis than it is today, even with the support of sound scientific investigation. De Quincy's remarks are as follows:

> Though not exactly in the same circumstances as Kate (the Spanish nun), or sleeping on a declivity of the Andes, I have known, or heard substantially repeated, the cases of many ladies besides Kate who were precisely in the same critical danger of perishing for want of a little brandy. A dessert spoonful or two would have preserved them. Avaunt, you wicked temperance medallist! Repent as fast as ever you can, or perhaps, the next time we hear of you, *anasarca* and *hydrothorax* will be running after you to punish your shocking excesses in water. Seriously, the case is one of constant recurrence, and constantly ending fatally from unreasonable and pedantic rigor of temperance. The fact is, that the medical profession composes the most generous and liberal body of men amongst us; taken generally, by much the most enlightened; but professionally, the most timid. Want of boldness in the administration of opium, &c., though they can be bold enough with mercury, is their besetting infirmity; and from this infirmity females suffer most. One instance I need hardly mention, the fatal case of an august lady, mourned by nations, with respect to whom it was said and is the belief of multitudes to this hour (well able to judge) that she would have been saved by a glass of brandy; and her attendant, who shot himself, came to think so too late — too late for her, and too late for himself. Amongst many cases of the same nature which personally I have been acquainted with, twenty years ago, a man, illustrious for his intellectual accomplishments, mentioned to me that his own wife, during her first or second confinement, was suddenly reported to him by one of her female attendants, (who slipped away unobserved by the medical people,) as undoubtedly sinking fast. He hurried to her chamber, and saw that it was so. The presiding medical authority, however, was inexorable. "O, by no means," shaking his ambrosial wig, "any attempt at this crisis would be fatal." But no authority could overrule the concurrent testimony of all symptoms and of all unprofessional opinions. By some pious falsehood, my friend smuggled the doctor out of the room, and immediately smuggled a glass of brandy into the poor lady's lips. She recovered with magical power. The doctor is now dead, and went to his grave under the delusive persuasion that not any glass of brandy, but the stern refusal of all brandy was the thing that had saved his collapsing patient. The patient herself, who might naturally know something of the matter, was of a different opinion. She sided with the factious body around her bed, (comprehending all besides the doctor,) who felt sure that death was rapidly approaching, barring that brandy. The same result in the same appalling crisis I have known repeatedly produced by twenty-five drops of laudanum. An obstinate man will say, "O, never listen to a non-medical man like this writer. Consult, in such a case, your medical adviser." You will, will you? Then let me tell you you are missing the very logic of all I have been saying for the improvement of blockheads; which is, that you should consult any man *but* a medical man, since no other man has any obstinate prejudice of professional timidity.

It should be noted that since preparing to record the above observations and quotations I have found that the *Oxford Dictionary* gives 1751 as the earliest date of the recorded use of *antiseptic.* Its Greek etymology suggests that the word was applicable to anything calculated to counteract a noxious tendency; an example is given of such a metaphorical use. It is perhaps a reasonable guess that the first use of *antiseptic* was only as an adjective and that as a noun, referring to substances having an antiseptic effect, it dates from the time of Lister. De Quincy might be said to have had an antiseptic influence on the fanaticism of temperance advocates and perhaps, also, on the obstinate dogmatism of the medical profession!

CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 42031

PRESENTATION OF CASE

A fifty-five-year-old man entered the hospital because of difficulty in breathing.

About four months previously he first noted diminished appetite and dysphagia. There was no nausea, but ingested food was vomited shortly after it was swallowed. Two months before entry a hacking, progressively worsening cough productive of mucoid sputum as well as persistent exertional dyspnea, orthopnea and frequent wheezing were noted. There was no chest pain, chills or fever. A couple of weeks later the sputum had increased in amount, appeared yellow and was intermittently blood tinged. The dysphagia worsened so that only soft solid and semisolid food could be ingested. Swelling of the feet was noted. One month before admission the patient was admitted to another hospital, where he remained for three weeks. X-ray films showed a mass involving the posterior mediastinum and left lung. Three sputum examinations were negative for acid-fast bacilli. There had been an estimated 30-pound to 40-pound weight loss since the onset of symptoms. He had been a heavy cigarette smoker for more than twenty-five years.

FIGURE 1. *Lateral View of the Chest.*
The mass appears partially interposed between the esophagus and the trachea and displaces the trachea anteriorly. A defect is present in the anterior aspect of the esophagus at the level of the mass.

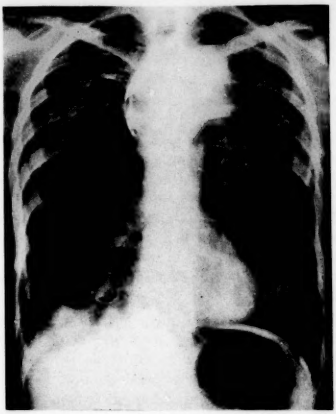

FIGURE 2. *Posteroanterior View of the Chest, Showing a Large Mass in the Superior Mediastinum Indistinguishable from the Aorta.*
There is a right-sided pneumothorax and evidence of atelectasis and pneumonitis at the right base.

Physical examination revealed a cachectic, cyanotic man who was in severe respiratory distress with an almost constant cough and inspiratory and expiratory wheezes. The right pupil was greater than the left; both were round and reactive. Extraocular movements were normal. Examination of the pharynx was negative. The neck veins were distended and filled from above. One observer felt a few small hard lymph nodes in the left supraclavicular region. The trachea was deviated to the right. Both leaves of the diaphragm moved with respiration. Examination of the lungs anteriorly revealed dullness with diminished tactile fremitus and breath sounds on the right; posteriorly, there was dullness over the left upper lobe and increased resonance over the left lower lobe. Examination of the heart was unsatisfactory because of respiratory distress. The liver edge was palpable 4 fingerbreadths below the right costal margin. Slight bilateral costovertebral-angle tenderness was noted. At the anterior superior medial pole of the right

testis there was a nontender, slightly firm mass measuring 1.5 cm. by 2.5 cm. There was a suggestion of clubbing of the fingers and toes. There was +++ pitting edema up to the knee on the left and to the midleg on the right. Rectal examination was negative.

The temperature was 99.6°F., the pulse 84, and the respirations 35. The blood pressure in the right arm was 100 systolic, 70 diastolic, and that in the left arm 110 systolic, 68 diastolic.

The urinary sediment contained 10 to 20 yeast cells, 0 to 3 white cells and a few bacteria per high-power field; otherwise, the urine was normal. Examination of the blood revealed a hemoglobin of 14.5 gm. per 100 ml. and a white-cell count of 30,700, with 87 per cent neutrophils. X-ray films of the chest demonstrated a mass in the superior mediastinum lying between the trachea and esophagus, causing marked obstruction of both trachea and esophagus and extending into the superior lung fields bilaterally (Fig. 1 and 2). Both lungs showed increased vascularity. There was a patchy area of increased density at the right-lung base. Both leaves of the diaphragm moved normally. An abdominal film was normal. No acid-fast bacilli were demonstrable in the sputum; culture grew out abundant *Haemophilus influenzae* and alpha-hemolytic streptococci, moderate beta-hemolytic streptococci, a few nonhemolytic streptococci and rare coliform bacilli; cytologic examination for malignant cells was unsatisfactory.

The patient died on the second hospital day.

Differential Diagnosis

Dr. J. Gordon Scannell*: We are not told the manner of the patient's death, which perhaps might contribute to the diagnosis. In summary, this man of middle age had a large mediastinal mass that had led to clear-cut tracheal, esophageal and venous obstructions. Before discussing this further, may I see the films, which so often look different from the description in the protocol?

Dr. Richard V. Wilson: In the two films from the other hospital taken a month before admission here, the measurements of the mass were no different from those in the films taken in our hospital. The trachea and esophagus are best delineated in the lateral views. The trachea is markedly narrowed. The mass is projected between the esophagus and trachea in the lateral view (Fig. 1). The bronchi are not too distinctly seen but do not seem to be compressed. On the films taken in the other hospital there is no air in the pleural cavity; in ours there is a pneumothorax on the right. The thin streak of air in the right pleural cavity between the lung and mediastinum indicates that the mass is not in the right lung (Fig. 2). I cannot differentiate the mass from the great vessels, including the aorta. I do not definitely see the aorta until I see the lower descending aorta. I do not see the aortic knob at any point. I believe the ascending aorta is here, but I am not absolutely certain of that. There is no definite calcification within the mass. The filling defect of the esophagus, I think, is a "red herring" and probably food. Very little barium passed beyond the mass, for there is obstruction here, with dilatation of the esophagus above the obstruction. Certainly, there is a marked narrowing of the trachea. The movement of the diaphragm was not mentioned in the report of the fluoroscopy. The left leaf is slightly higher than the right, but I doubt if that means anything because the film was taken when there was a great deal of air in the stomach. There is infiltration at the right base, which I believe is aspiration pneumonia. This shadow may be a tiny cavity.

Dr. Scannell: Do you know whether the mass was pulsatile?

Dr. Wilson: I do not; there is no comment about that in the fluoroscopic note.

Dr. Scannell: It is surprising that there is a pneumothorax. It does not help me diagnostically, but it does help in ruling out a lesion of the lung parenchyma. Do you think that the mass is between the trachea and the esophagus or posterior to them and pushing the esophagus to the right?

Dr. Wilson: No; it is not between the two. The esophagus is pushed to the right, the mass being on the same level and slightly anterior to the esophagus, and the trachea is pushed anteriorly.

Dr. Scannell: Is there any change in the vertebral bodies such as erosion or displacement?

Dr. Wilson: The best film of the thoracic spine — the one taken in the other hospital a month before death — shows no erosion. In our films the vertebral bodies are not clearly seen, but there is nothing that looks like erosion.

Dr. Scannell: In the differential diagnosis of this mass, the first possibility to cross my mind is an aneurysm of the arch of the aorta since by x-ray examination all the criteria of it are satisfied: the mass is inseparable from the arch of the aorta; it is in the posterior mediastinum; and it displaces the esophagus to the right and the trachea forward as an aneurysm of the descending portion of the aorta will do. Furthermore, although it has grown to considerable size, it has not apparently invaded the structures in the mediastinum. So far as I can tell, the recurrent nerve, which I would have expected to be affected by an aneurysm, is not disturbed. The mass does not, I am fairly certain, originate in the lung field. There are a few other things that I should like to know. I should like to know, of course, what the result of the blood Hinton test was. I assume that the patient died before that was reported and therefore that the physicians taking care of him did not have access to that information either. I should like to know whether on physical examination there was a tracheal tug,

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which if this was an aneurysm, should have been quite obvious.

The history is compatible with an aneurysm that was exerting pressure on the trachea and esophagus and causing perhaps some bleeding into the trachea either by leakage or from pressure alone. In addition an aneurysm, particularly in the superior mediastinum, may produce the venous obstruction that this patient had. I suppose the most common benign cause of a superior-vena-cava syndrome is an aortic aneurysm.

If it was not an aneurysm, what is it likely to have been? A diffuse neoplasm in the mediastinum usually involves the phrenic nerves, which were not involved in the case under discussion since both leaves of the diaphragm seemed to move. I should expect a diffuse malignant process to cause more anemia than this patient had. That he had lost weight is true, but he was not anemic. If a malignant process originates in the trachea, it gives rise to more bleeding or respiratory symptoms than this patient had. It is difficult to believe that this was a tracheal carcinoma. Usually, a tracheal carcinoma does not grow to this size before killing the patient, nor does it have this shape. It could have been a primary bronchogenic carcinoma with mediastinal lymph-node involvement; however, I should expect more parenchymal involvement. I think, as Dr. Wilson has said, that the density in the right base represented pneumonitis, rather than a primary carcinoma. Even if it was a carcinoma I should be surprised to see this much involvement of the posterior mediastinal lymph nodes. Furthermore, such a rapid evolution of carcinoma in the lung suggests an oat-cell carcinoma. The x-ray picture is not that of a centrally placed oat-cell carcinoma. It could have been carcinoma of the esophagus, but, again, it is almost inconceivable that one would grow to this size without killing the patient. With a carcinoma of this size of either the trachea or the esophagus one would expect a fistula between the two.

Among the other malignant tumors of the mediastinum, lymphoma crosses my mind. Lymphoma is more common in the anterior mediastinum and only rarely forms a large solitary tumor. Although it is a possibility, I think that the evidence for an aneurysm is much better.

Malignant degeneration could have occurred in a benign mediastinal tumor, but with that, one would expect more evidence of invasion of, rather than merely encroachment upon, the mediastinal structures. The tumors in the posterior mediastinum are usually neurogenic in origin. Malignant neoplasms in this area tend to throttle a patient rather than to encroach upon and displace the structures laterally. I am inclined to treat this mediastinal mass as being vascular in origin, probably an aneurysm of the descending portion of the arch of the aorta.

DR. WILSON: Would you consider a substernal thyroid gland?

DR. SCANNELL: A substernal thyroid gland may be behind the great vessels. I suppose it could mimic this appearance. I think it would be most unusual for it to reach this size and be such a lethal mass.

A PHYSICIAN: Would you consider an abscess from a ruptured diverticulum?

DR. SCANNELL: The thought did not occur to me. There was no history of diverticulum or of instrumentation. I have never seen an abscess from an esophageal mass localized in the mediastinum that did not contain air and did not give more evidence of diffuse mediastinitis. This was localized.

DR. JACOB LERMAN: Does not the x-ray film taken in the other hospital a month before death, as well as the one taken here, show some infiltration in the right base?

DR. WILSON: That is true; it is more advanced on our films.

DR. LERMAN: That was a pneumonic process?

DR. WILSON: I think so.

DR. SCANNELL: I should agree. One of the points that bothers me is that it was on the right instead of the left. I should expect more interference with the left bronchial tree. That was one of the facts that I chose to ignore.

DR. WILSON: I should expect, by the time of admission, to see bilateral pneumonitis if the patient had had aspiration pneumonitis a month before, when the other films were taken. The position of the pneumonitis on the right may be explained by the fact that the right main bronchus is more vertical than the left. Incidentally, I cannot explain the filling defect in the esophagus as a carcinoma, for I have never seen a primary carcinoma of the esophagus displace the esophagus.

A PHYSICIAN: Do you think that the tumor of the testicle is a "red herring?"

DR. SCANNELL: I did — along with the "herring" in the esophagus.

DR. ALLAN SANDLER: On the wards, we believed that the two best possibilities were carcinoma of the lung and carcinoma high in the esophagus. Although this man had mediastinal symptoms first and then pulmonary, I thought that carcinoma of the lung was the best bet because of the history of smoking, cough, hemoptysis, hepatomegaly, clubbing and fulminating downhill course in a period of three months. I believe clubbing is commonly found with carcinoma of the lung and rarely if ever seen with metastatic disease of the lung or primary disease of the mediastinum. The mass in the testis was soft and almost fluctuant, and we too thought that it was a "red herring."

CLINICAL DIAGNOSIS

?Bronchogenic carcinoma, with obstruction of esophagus and trachea.

DR. J. GORDON SCANNELL'S DIAGNOSIS

Aneurysm of descending portion of arch of aorta.

Anatomical Diagnoses

Carcinoma of lung, left upper lobe, with widespread mediastinal extension and extension into trachea and esophagus.
Pulmonary embolism and infarction, right.
Hemochromatosis of liver and pancreas, incidental.

Pathological Discussion

Dr. Winfield S. Morgan: The primary lesion in this case was found to be a plaquelike mass arising from the apical posterior bronchus of the left upper lobe. This tumor had eroded the bronchus, had replaced a large portion of the left upper lobe and had extended widely throughout the mediastinum. In the posterior mediastinum it surrounded the great vessels and protruded into the trachea and esophagus. The tumor encroaching on the esophagus was, I am sure, the nodule called a "red herring" in the x-ray film. The mucosa of the esophagus stretched in a thin layer over the tumor, and in a few areas it had become ulcerated.

Microscopically, the tumor proved to be a highly malignant undifferentiated carcinoma consisting of pleomorphic cells, with large bizarre hyperchromatic nuclei having no fixed pattern whatsoever.

Dr. H. L. Heyl: Did you look at the lymph nodes?

Dr. Morgan: The lymph nodes were apparently normal, and there was no tumor outside the chest. The right lung contained a number of small infarcts and corresponding emboli. There were also areas of organizing pneumonitis throughout the lungs. Could the shadow in the right base have been one or more infarcts, Dr. Wilson?

Dr. Wilson: It does not have the typical appearance of an infarct.

Dr. Benjamin Castleman: I believe that when there are more than one infarct they may be superimposed on each other so as to give almost any kind of shadow in the lung.

Dr. Lerman: Were those tumor emboli?

Dr. Morgan: No; they were the usual bland emboli, and there were thrombi in the popliteal veins.

Dr. Wilson: Were the emboli scattered through the right lung or only at the base?

Dr. Morgan: They were scattered throughout the right lung, but were confined to it; there were none in the left.

Dr. Scannell: Do you think that you could identify the primary tumor on the film, Dr. Wilson?

Dr. Wilson: No; not the primary tumor. However, in retrospect, I believe I can see marked narrowing of the left main-stem bronchus in the oblique view. Also, it is extremely rare for a vascular lesion to cause this much separation of the esophagus and trachea.

Dr. Morgan: There was an incidental finding in this case. The liver was somewhat heavy, weighing 1900 gm., and seemed tough on gross examination. The microscopical sections showed a mild cirrhosis and a heavy deposition of hemosiderin in the cells of the liver, and also of the pancreas, that were consistent with the diagnosis of hemochromatosis.

A Physician: What was the testicular mass?

Dr. Morgan: It was a benign cyst of the epididymis.

CASE 42032

Presentation of Case

A sixty-three-year-old woman entered the hospital with a complaint of "gall-bladder pains."

Fifteen years previously she had an illness that was said to have involved the gall bladder. Hypertension was also noted. She was hospitalized for several weeks, after which she remained well until three years later, when jaundice and mild right-upper-quadrant distress were noted. A gallstone was visualized on x-ray examination. Operation was advised but refused. The jaundice and right-upper-quadrant pain subsequently disappeared. Two years before admission dyspnea on exertion was noted, and she was given digitalis with improvement. Two months before entry she suddenly had spontaneous, severe, sharp, intermittent, nonradiating right-upper-quadrant pain relieved by aspirin, and soreness in the right flank. There was no associated fever, nausea, vomiting, jaundice or change in color of the urine. The stools were said to have been "light colored." One week later a similar type of pain occurred in the left upper quadrant. This pain worsened while the right-upper-quadrant pain diminished. She had not noted recent weight loss, change in bowel habits or melena. There was no history of alcoholism. She had been taking 0.1 mg. of digitoxin daily, but no other medications.

Physical examination revealed a pale, well nourished woman. The optic fundi showed minimal arteriovenous nicking and tortuosity. There were several xanthomas beneath the lower eyelids. A small, shotty lymph node was felt in the left supraclavicular region. The lungs were clear. The heart was enlarged to the left anterior axillary line. There was atrial fibrillation, with an apical pulse rate of 142. The aortic second sound was louder than the pulmonic. No murmurs were heard. Abdominal examination revealed bulging flanks without a detectable fluid wave. The liver edge was palpable 2 fingerbreadths below the right costal margin. An ill defined, firm, midabdominal mass, with an irregular surface, appeared to occupy the entire epigastrium. In the left upper quadrant there was a slightly tender, movable mass with rounded edges. There was + ankle edema. Pelvic and rectal examinations were negative.

The temperature was 98°F., the pulse 130, and the respirations 16. The blood pressure was 210 systolic, 100 diastolic.

The urine gave a brown test for sugar and a negative test for acetone. Examination of the blood revealed a hemoglobin of 12 gm. per 100 ml. and a white-cell count of 9500, with 65 per cent neutrophils and 23 per cent band forms. The total protein was 7.5 gm., the albumin 3.3 gm., the globulin 4.2 gm., the fasting blood sugar 229 mg., and the bilirubin 1 mg.

FIGURE 1. *Intravenous Pyelogram.*
The left kidney is displaced downward by the large spleen. The liver is also somewhat enlarged.

per 100 ml., the amylase 12 Russell units and the alkaline phosphatase 7.9 units. Bromsulfalein retention was 30 per cent. The serum nonprotein nitrogen, electrolytes and prothrombin time were normal. A stool specimen was normal in color and gave a negative guaiac test. An electrocardiogram showed atrial fibrillation, with a ventricular rate of 140 to 150 and sagging ST segments in Leads 1, 2, aVL and V_5 and V_6. An x-ray film of the chest demonstrated cardiac enlargement, chiefly of the left ventricle, and a slight degree of pulmonary vascular congestion. The spleen extended down to the midportion of the third lumbar vertebra. An intravenous pyelogram revealed good concentration and prompt excretion of Diodrast bilaterally. There was first-degree ptosis of the left kidney, apparently secondary to splenomegaly (Fig. 1). The right kidney showed several dilated calyxes and thinning of the cortex in the midportion. Several calcifications were noted adjacent to the uterus in the right pelvis and in the right midabdomen. A barium-enema examination revealed multiple diverticula and slight pressure on the splenic flexure caused by an enlarged spleen.

The pulse rate returned to normal with digitoxin and Cedilanid therapy, and the blood sugar was controlled with insulin.

On the eighth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. N. JOEL EHRENKRANZ*: In summary this sixty-two-year-old woman, at approximately the age of forty-eight, had an illness that was said to have involved the gall bladder; three years later she had an episode of jaundice and mild right-upper-quadrant distress, and a gallstone was visualized on x-ray examination. I am not told the degree of jaundice or the duration of the hospitalization, but that episode presumably fits with cholecystitis and cholelithiasis rather than an infectious hepatitis. Two years before admission dyspnea was first noted, and the picture suggestive of hypertensive cardiovascular disease, with atrial fibrillation and mild failure, subsequently developed.

Aside from this I must assume that the patient was in relatively good health until two months before admission to the hospital, when she suddenly experienced right-upper-quadrant pain. This pain was suggestive of gall-bladder disease, particularly since the patient, who had had previous experience in making her own diagnosis, entered the hospital saying that she had "gall-bladder pains." On the other hand it could have been pain arising from the liver. She had an episode of left-upper-quadrant pain that was similar in nature, nonradiating, sharp, severe, intermittent and more or less colicky and appeared while the right-upper-quadrant pain was diminishing. What could the origin of this pain have been? Conceivably, it resulted from some change in the pancreas. The pain did not radiate to the back, and there was no other evidence of acute pancreatitis or previous episodes of pancreatitis, so I must put this low on my list. This pain may have been due to perisplenitis secondary to involvement of the portal vein and enlargement of the spleen, or since she was fibrillating, she may have tossed small emboli to the spleen and had an episode of perisplenitis secondary to splenic infarct. It is also possible that this pain arose from the liver and was connected with the huge epigastric mass and the left lobe of the liver, which was extending across the midline.

Were there any other gastrointestinal symptoms such as nausea or vomiting or an alteration of the appetite? On physical examination was this mass felt to be contiguous with the liver and was it pulsating?

DR. PERRY J. CULVER: From the time that I saw this patient she had a wonderful appetite; I think she had had it previously. On physical examination my impression was that the mass was contiguous with the liver. Dr. Donaldson also examined her.

DR. GORDON A. DONALDSON: I could not map

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out the liver as such; there was a mass, probably contiguous with it.

DR. EHRENKRANZ: I think I shall make the diagnoses unrelated to the present illness and then dismiss them. The laboratory evidence of diabetes was well substantiated. She appeared to have moderate hypertensive cardiovascular disease, and she probably had slight decompensation secondary to the arrhythmia.

I shall now concern myself with what was going on in the abdomen, noting the presence of the enlarged lymph node in the left subclavian fossa. The patient had pains in the abdomen, first on the right and then on the left, a mass in the left upper quadrant, which I interpret as a palpable spleen, and a mass in the midepigastrium that was thought to be contiguous with the liver. Previously, she had been in good health except for the dyspnea and had an excellent appetite. The studies of the function of the liver revealed a moderate decrease in the serum albumin and moderate elevation in the globulin. The amylase was normal. There was an elevation of the alkaline phosphatase, increased bromsulfalein retention and no evidence of jaundice either clinically or chemically. The x-ray films are valuable from a negative standpoint. I was told that a gastrointestinal series did not reveal any change; obviously, that would be of major importance in the detection of an epigastric mass. May I see the x-ray films now, Dr. Hanelin?

DR. JOSEPH HANELIN: The films of the chest taken elsewhere about a month before the second admission show considerable enlargement of the heart, chiefly of the left ventricle, but there is a suggestion of asymmetrical prominence of the left atrium. The pulmonary vessels at the lung roots are slightly engorged. There is no pleural fluid and no evidence of pulmonary edema. The plain films of the abdomen show enlargement of the spleen; its tip is about 4 cm. from the iliac crest. The liver also appears to be increased in size. The left kidney lies low and is probably displaced downward by the enlarged spleen. The pyelogram demonstrates good renal function bilaterally (Fig. 1). There is not as good drainage of the renal collecting system on the right as on the left side, but I do not see any point of obstruction nor can I be certain of any intrinsic renal lesion. The bladder is slightly indented on the right side, and there is some calcification in this area, which probably is within a uterine fibroid. Two larger calcifications in the right lower portion of the abdomen overshadowing the ilium may represent a number of things but are most probably lymph nodes. The barium-enema examination shows no intrinsic lesion other than diverticula. The transverse colon lies low.

DR. EHRENKRANZ: Is the transverse colon being pushed down by a mass?

DR. HANELIN: I see no evidence of indentation by a mass. The patient tends to be low slung so this position of the colon may be normal. The films of the gastrointestinal examination show nothing intrinsic in the stomach; the duodenum is pushed toward the left side, possibly as the result of enlargement of the liver. The duodenum seems to be normal.

DR. EHRENKRANZ: Are there gallstones?

DR. HANELIN: I cannot be sure of opaque stones. No gall-bladder series was done.

DR. EHRENKRANZ: Is there any evidence of Paget's disease?

DR. HANELIN: No; there is not.

DR. EHRENKRANZ: The differential diagnosis of hepatosplenomegaly and an epigastric mass in a middle-aged woman with diabetes and heart disease leads me to the following considerations. I think I can mention and then dismiss Hodgkin's disease, sarcoidosis and amyloidosis, for I see nothing in the x-ray examination and physical findings that would support these diagnoses. Cirrhosis leaps to mind, but in the absence of an alcoholic history or a history of exposure to hepatotoxins, Laënnec's, toxic and postnecrotic cirrhoses may be ruled out. She had a mild degree of heart failure, but I do not think it was of such long standing as to cause cardiac cirrhosis. The diabetes with liver disease raises the question of hemochromatosis. The fact that this is an unusual disease in women and the absence of pigmentation — the patient was described as being pale — lead me away from this possibility. She had had episodes of cholecystitis and cholelithiasis; therefore, it is not unreasonable to assume that part of the hepatosplenomegaly and slight elevation in serum globulin may have represented biliary cirrhosis. The epigastric mass described as being attached to the liver conceivably may have been a cyst of the pancreas or carcinoma of the stomach, but there was no evidence to support these ideas. The facts that it was not pulsating and was attached to the liver certainly do not lead me to the diagnosis of an aneurysm of the abdominal aorta.

I come to the conclusion that the mass most probably represented a malignant tumor. There are several possible primary sites. The calcification in the region of the right ovary or uterus suggests this as a possibility. I shall accept Dr. Hanelin's interpretation that a fibroid was the source for the calcification and dismiss it. There were slight changes in the kidneys, particularly the right kidney, — dilated calyxes and thinning of the cortex were described, — but there is no evidence of a tumor on the x-ray film. Is that correct, Dr. Hanelin?

DR. HANELIN: That is correct.

DR. EHRENKRANZ: I suppose, in view of the history of diabetes, chronic pyelonephritis, which is common in women with diabetes, would account for the renal x-ray changes, so I think they may be dismissed.

The negative barium-enema examination, except for the diverticulosis, the normal gastrointestinal series, the normal roentgenogram of the chest and the normal breasts make carcinoma arising in the bowel,

stomach, lungs or breasts remote. A small primary lesion in the lung or bowel could be missed, but one would expect that an anemia or some other abnormality would have been present. On the basis of what is given both by history and in the x-ray findings, the postulate that carcinoma arose in one of these sites is not tenable.

Hepatoma and bile-duct carcinoma are possibilities. The latter might be more likely in view of the patient's sex; the former lesion is characteristically more common in men. I should not expect a history of rather good health until a short time before admission, with good appetite and no evidence of a progressive downhill course — although ascites was indicated by the bulging flanks.

I am left with the diagnosis that I prefer: a carcinoma arising in the gall bladder with metastases to the liver, both by direct extension and by hematogenous spread. In support of this is the fact that this carcinoma occurs frequently in patients with a previous history of gallstones. The various series give incidences between 60 and 95 per cent with biliary calculi.[1] The lesion is more common in women, particularly in this age group, the ratio being approximately 4:1, and the patients not infrequently appear to be in relatively good health. Anemia, leukocytosis and evidence of massive ascites or even jaundice do not necessarily appear until rather late in the course of the disease.[2] I should prefer for that diagnosis to have a story of anorexia or some alteration in the food intake, but it is conceivable that this patient was a stoic or was not given to accurate observation in this sphere. I think I shall rest my case with this diagnosis.

Dr. Culver: Would you tell us why you believe that postnecrotic cirrhosis was ruled out?

Dr. Ehrenkranz: I do not believe that it was completely ruled out. I should like to know whether or not there was any cause for it. That would alter my view.

Dr. Culver: A great many of the patients with esophageal varices that we see here have no history of malnutrition, of anorexia or of previous jaundice, but at the time of either liver biopsy or of a shunt operation they have a fairly severe postnecrotic cirrhosis.

Dr. Ehrenkranz: One could make a good case for that diagnosis in view of the previous jaundice, which might have been caused by infectious hepatitis. She may have had a history of malnutrition without its being noted. I wonder if the liver-function tests should not have been more awry. If more tests were done, they might have helped us. If this was an advancing cirrhosis, why was the liver not smaller, rather than manifesting a mass suddenly? I assume that the mass had not been noted previously.

Dr. Culver: I do not know about the past physical examination.

A Physician: Since there was a background of gall-bladder disease, with a hepatic mass and diabetes, would you consider a pancreatic cyst?

Dr. Ehrenkranz: I considered that. I should like to have some evidence in a gastrointestinal series that such a cyst widened the loop of the duodenum. If a cyst was as large as this mass was, I should expect signs of pancreatic insufficiency.

Dr. Jacob Lerman: How would you explain the large spleen on the basis of carcinoma of the gall bladder?

Dr. Ehrenkranz: There are two possible explanations: one is biliary cirrhosis, which may in late stages give rise to portal hypertension, and the other is invasion of the portal bed, causing splenomegaly.

Dr. Lerman: Without ascites?

Dr. Ehrenkranz: She had bulging flanks.

Dr. W. Warren Point: Is it not true that carcinoma of the gall bladder rarely spreads very far — does not involve the liver and other organs — without causing massive jaundice in the early stages?

Dr. Ehrenkranz: Perhaps anticipating your question, I looked this up in the literature. In the 55 cases of primary carcinoma of the gall bladder reported by Kirshbaum and Kozall[1] preterminal jaundice occurred in no more than 60 per cent of the patients, and that was caused by obstruction at the porta hepatis. Other series give about the same figures. I think that there may be diffuse involvement of the liver without jaundice.

Clinical Diagnosis

?Lymphoma of liver.
?Carcinomatosis, with ascites.

Dr. N. Joel Ehrenkranz's Diagnosis

Carcinoma of gall bladder, with liver metastasis.

Anatomical Diagnoses

Cirrhosis of liver, posthepatitic type.
Splenomegaly.
Ascites.

Pathological Discussion

Dr. Edgar B. Taft: The operation was exploratory. Dr. Donaldson, can you tell us what Dr. Arthur W. Allen found at the operation?

Dr. Donaldson: I can tell you about the preoperative opinion. This patient worried us as much as she has the group here. As a matter of fact I think that she was sicker than the protocol would lead one to believe, and contrary to the note, she was not particularly well nourished. We knew that she had severe heart disease. We suspected that she had a great degree of liver insufficiency and gallstones. The mass attracted the attention of the surgeons of course, and the exploration was done to find out what this mass was. I think we were led astray — and Dr. Ehrenkranz may have been led astray —

by the description of the liver. The liver edge could be felt laterally, and the mass more medially was thought to be part of the liver preoperatively. Among other diagnoses before operation lymphoma was seriously considered.

DR. TAFT: There is one note by the house officer that mentioned carcinoma of the pancreas as a possibility. I think most of the physicians who saw this patient considered that she had a malignant tumor. At the time of operation, however, when Dr. Allen opened the abdomen, there was a gush of a moderate amount of clear, yellow ascitic fluid. Then the liver presented itself; the midepigastric mass proved to be the left lobe of the liver. The liver was firm and irregularly nodular, with large and small nodules. The spleen also was enlarged. Careful exploration of the abdomen failed to give any evidence of tumor. The gall bladder was small and contained two or three stones by palpation, but Dr. Allen did not believe that it was enough indication to remove the gall bladder, so that he did not do so. Instead he took a biopsy of the liver. On microscopical examination some of the nodules (Fig. 2) were quite large, with good preservation of the liver architecture within them; some of the nodules had the appearance of areas of regeneration of liver cells and did not have the usual lobular architecture. Thin fibrous septums separated the parenchymal lobules. The liver cells appeared to be healthy and full of glycogen and showed no abnormality. There was no evidence of bile stasis or of biliary cirrhosis.

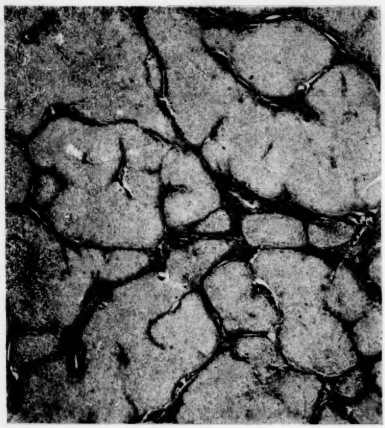

FIGURE 2.

It is my opinion that the episode of jaundice and pain three years before admission represented an attack of hepatitis and that this was the end result of that infection. That presumptive attack of hepatitis was probably completely unrelated to the gall-bladder disease. There have been enough descriptions in the literature of hepatitis leading to this type of cirrhosis so that I think most physicians agree that this form of cirrhosis may be a sequel of hepatitis and a complication to be concerned about in patients who have had this disease.

DR. BENJAMIN CASTLEMAN: Dr. Gall, formerly in our laboratory and now at the University of Cincinnati, has collected a large series of cases of cirrhosis with a picture like this — that is, one in which the architecture of the liver is still preserved and in which the fibrous bands that extend between portal spaces are thin and almost abortive.[3] He proposes to call this type of cirrhosis posthepatitic cirrhosis rather than postnecrotic; in the latter, there are large broad and irregular bands of fibrosis as evidence of previous large areas of necrosis. In the usual case of viral hepatitis the inflammatory reaction is in the portal area, and although usually this clears completely, in some cases the residua may terminate as a portal cirrhosis. Dr. Gall tells me that in a very high percentage of these cases he has been able to elicit a history of previous hepatitis.

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POLIOMYELITIS VACCINATION APPRAISED

IN the December 1, 1955, issue of the *Journal* the Poliomyelitis Advisory Committee to the Massachusetts Department of Public Health, on account of wide misunderstanding of its position on the poliomyelitis vaccine program, made a public statement in the form of a letter to the editor. It indicated clearly that its approval of such a program had been deferred and not canceled and that a final decision for 1956 would be made well before large-scale vaccination would need to be initiated. Meanwhile, the evaluation of poliomyelitis vaccination in Massachusetts in 1955, by a special committee of the Department operating under a grant from the National Foundation for Infantile Paralysis, Incorporated, was under way and is reported in this issue.

The attitude of the Advisory Committee continued not unexpectedly to be variously misinterpreted, largely, although probably not exclusively, by many whose utterances seemed to be based on prejudice and tinged with emotion. Encouraging indeed to those who are trying to view the problem in all its aspects was an editorial in the *Boston Herald* of December 20 expressing approval of the Advisory Committee and confidence in its judgment. This was in marked contrast to the pronouncements of a local sportswriter, who, dismissing lightly the serious study that the Committee had made of the matter and ignoring the exceptionally high competence of its members, gave his unqualified blessing to the vaccine (or serum).

Further information on the whole involved subject was published in last week's *Journal* in a letter from Dr. Hart E. Van Riper, medical director of the National Foundation for Infantile Paralysis. Dr. Van Riper discussed the epidemic of 1955 as it affected the New England area and particularly Massachusetts, and emphasized the impressive part played by the Foundation in combating it. Dr. Van Riper's references to poliomyelitis vaccine were phrased in the moderate and objective terms that would be expected from a scientifically trained and open-minded physician. Appreciation of his point of view and of the March of Dimes itself was expressed in an accompanying editorial.

The report of the study committee, published as a special article elsewhere in this issue of the *Journal*, is a careful analysis of the experience in Massachusetts with the 1955 epidemic of poliomyelitis with special reference to the effect on it of the vaccine. No evidence was discovered that the vaccine had given rise to any cases in this state. A study of its effectiveness revealed that attack rates among both vaccinated and unvaccinated children were much higher than those reported by Francis after the field trials in 1954. Thus the attack rate for unvaccinated children was found to be 198.2 per 100,000; for those who had received 1 injection, 94.5 per 100,000;

and for those who had received 2 or more doses, 66.4 per 100,000. The single dose, therefore, seems to be nearly as effective as were 3 injections. The effectiveness of the vaccine for all cases of poliomyelitis was 53 per cent and for paralytic cases 60 per cent.

The questions of the ultimate safety of the vaccine, of its year-by-year effectiveness, of the duration of immunity, of carrier states and of latent sensitization remain to be answered. It is to be borne in mind also that the vaccine itself has undergone considerable modification since it was first introduced, and these modifications must be considered *each* time its value is reviewed by the Advisory Committee. The balance between safety and effectiveness, for instance, may be so fine that increased safety is purchased at too great a loss of effectiveness. The wisest counsel that can be given at this point is for the profession and the public to continue to put their confidence in the Committee, which has courageously maintained a completely objective attitude from the beginning.

DIVIDING THE CHARITY DOLLAR

FIGURES published by the United States Department of Commerce indicate that consumer spending amounts to about $1,363 annually for every man, woman and child in the country. Of this, 61 per cent goes for food, shelter and clothing. Of the remaining 39 per cent, $82 apiece is spent for alcoholic beverages, $49 for tobacco, and $68 for "medical care and death expenses." Only $13.53 is donated by the average person to religious and welfare activities. Of this, $1.80 goes to Red Feather services, community chests or united community funds, leaving $11.83 out of which must come donations to all other organized fund campaigns that compete with the Community Fund drive every fall.

Whether one's annual contribution to "charity" is $10 or $1,000, however, there is need for a rough yardstick by which to determine the proportionate amount that should reasonably go to any given individual cause.

It seems not unreasonable to expect that the average contribution to community fund drives should at least be doubled. If 30 per cent of one's giving were to such organizations, the community would benefit. The individual's sense of obligation will tell him how much to give to his church. The needs of various other special campaigns were summarized in these columns last May.* To reprint these figures may be helpful in deciding how to allocate what is left. Using poliomyelitis (the "March of Dimes") as a unit, and estimating the needs of other special disease funds by the number of victims involved, some such scale of relative importance as the following resulted, though it is realized that many worthy causes were not listed:

Poliomyelitis	1.0
Muscular dystrophy	2.0
Multiple sclerosis	2.5
Tuberculosis	4.0
Cerebral palsy	6.0
Cancer	7.0
Mental disease	25.0
Arthritis and rheumatism	75.0
Heart disease	160.0

This simply means that for every victim of poliomyelitis who needs help, there are 160 victims of heart disease, 75 with arthritis or rheumatism, 7 with cancer, and so on.

The particular emotional appeal of any one disease or group of persons affected may well lead one to increase his proportionate contribution to that disease or cause.

The editorial mentioned above was widely quoted and was widely misinterpreted. Its purpose was rather to demonstrate the general illogicalness of the free-for-all grab for the charity dollar than to persuade the charity-minded citizen to increase his heart-disease donation to 160 times what he gave to the March of Dimes. The *Journal* is heartily in favor of consolidated drives, as indicated by the title of the editorial: *"E Pluribus Unum."*

JOINT BLOOD COUNCIL

IT was announced in the fall that a joint blood council has been formed to co-ordinate blood-banking activities in the United States. This council is made up of 2 representatives each of the American Hospital Association, the American Society of Clinical Pathologists, the American Medical Association, the American Association of Blood Banks and the American National Red Cross. Regardless of the publicly avowed purpose of the organization, its intent is clear: to bring peace and harmony in what has been a troubled area — namely, the control of blood collection and distribution. This is definitely a step in the right direction, and such a committee may be able to go a long way in settling the differences that now exist. From that point of view medicine in general should be thankful that it has come into existence and look forward to an improvement in transfusion therapy on a national and, in many areas, on a local level.

A slightly more critical appraisal of the constitution of this council, however, leads to less optimism about its ability to achieve its objectives. In the first place, it represents 5 organizations, of which only 2 —the Association of Blood Banks and the Red Cross — are actually in the blood-banking field. The interest of the other 3 agencies is indirect — that is, their concern is limited to how blood-banking policies affect their individual members or medicine as a whole. Although the validity of the interest of these groups cannot be questioned, the benefit to be derived from their controlling the Council is open to argument. Among the 11 men who make up the

*Editorial. *E. pluribus unum. New Eng. J. Med.* **252**:783, 1955.

Council, only 4 officially represent the Red Cross and the Association of Blood Banks. Transfusion therapy, having become a highly specialized branch of medicine, should be controlled in the main by its own specialists — namely, blood-bank directors. A more effective make-up for the Council might be to have it predominantly controlled by active blood-bank directors and medical directors of the Red Cross, with a minority representation of other interested associations.

The same argument holds for the Executive Vice-President, who, although he has had experience in setting up blood-bank programs and was the first chairman of the committee on blood of the American Medical Association, is not a blood-bank director. As executive vice-president, he will guide the work of the Council and will occupy a position of which a cardinal qualification should be prolonged experience in the blood-banking field.

There are two more counts upon which the Council might be criticized. The first is its geographic location, which may be appropriate for the development of a civil-defense program but is poor from the point of view of arbitration of disputes and co-ordination of activities. A more central location in the Middle West would be preferable. Lastly, the essential weakness of the Council lies in the fact that it is entirely voluntary, that its members may withdraw if they wish and, hence, that its decisions cannot be binding. For it to be effective, the member associations should agree to be governed completely by its decisions and should be unable to withdraw without a two-thirds vote of their membership.

It can only be hoped that the present setup of the Council represents but an initial step in the right direction and that subsequent ones will result in a change in its constitution, control, direction and location so that it can better co-ordinate the activities of blood-collecting and distributing agencies in the United States.

WINGS OF SONG

It has been said, although perhaps more for dramatic effect than as a statement of positive fact, that there is nothing new under the sun. Consequently, it may be that in some unrecorded period or on a remote planet in a distant solar system, a world-famous symphony orchestra has brought some of the world's most honored music to a house packed with music-minded physicians, their wives and marriageable daughters.

Such was the privilege extended to the fellowship of the American Medical Association in Boston on December 1, when all who had secured tickets, free for the asking, met in Symphony Hall as guests of Winthrop Laboratories, Incorporated, for a specially arranged concert. Here, under the direction of its conductor, Dr. Charles Munch, the celebrated orchestra, observing the seventy-fifth year since its founding, lifted its audience on wings of song through the music of Mozart, Richard Strauss and Brahms.

As stated in his own brief introductory message in the program, Dr. Theodore G. Klumpp, now president of Winthrop Laboratories, had had his personal introduction to the Boston Symphony Orchestra during his student days at Harvard Medical School, when he was only one of a stream of Boston students to profit from the cultural advantages that the city had to offer. His recollection of these imperishable experiences inspired Dr. Klumpp to make this unusual and gracious offering to his medical colleagues from the country over.

The profession of medicine has become too readily accustomed to largesse from the pharmaceutical industry in the form of cocktail parties, television programs, elaborately packaged samples, unsolicited literature and multicolored advertisements, not always conservatively tailored to the mediums that they employ or in tune with the high purposes to which some of its representative firms are already partly dedicated. When the industry's resources in general are directed to unrestricted research, to the support of medical libraries and of orthodox education as well as to the exploration of new methods of instruction and to contributions on a level as high as that which Winthrop Laboratories has reached in this enterprise, then it makes itself truly a partner in the pursuit of medical ideals.

Dr. Klumpp deserves the thanks of all his fellow physicians, whether or not they were in Symphony Hall on the night of December 1.

A Yankee doctor has contrived to extract from sausages a powerful tonic, which he says contains the whole strength of the original bark; *he calls it the "Sulphate of Canine!" He anticipates a great popularity for it in New York city.*—Worcester Transcript.

Boston M. & S. J., *Jan. 25, 1855*

MASSACHUSETTS MEDICAL SOCIETY

GORDON MACKAY MORRISON

The life of Gordon Mackay Morrison, M.D., was filled with venturesome achievements and generous public service that stretched far beyond the usual routine of medical practice. He was born in 1896. During World War I he volunteered for the Royal

Flying Corps and received cadet training for this uncommonly hazardous service in Canada. Only brief apprenticeship was allowed since the high mortality among combat pilots made the demands for replacements urgent. Morrison reached the front in time to down one German plane before the war ended. While awaiting his discharge from the service, he won the heavy-weight boxing championship of the Royal Air Force, having learned to spar from his father, who was noted in East Boston both as a physician and as an amateur pugilist.

After these full-blooded adventures, it was hard to return to academic routine, but Morrison buckled down and graduated from Harvard College in 1921 and Tufts College Medical School in 1926. In spare time he coached football squads at Harvard, Williams, and in Iowa. Here, his success was so notable that Howard Jones, then of national prominence, asked Morrison to serve as his line coach in California. Instead, he took up a surgical internship at the Boston City Hospital where he later served, for over two decades, on the Visiting Staff. In 1954 he became acting chief surgeon of the Bone and Joint Service at the Hospital, but to the regret of all his associates, he was obliged to retire almost at once, on account of a suddenly manifested heart condition.

From 1929 to 1938, Morrison was associated with Dr. Frederick J. Cotton as assistant and then as partner. This drew him exclusively into the field of bone-and-joint surgery, which became his chief interest. He wrote a number of orthopedic papers, and he conducted a very successful consulting practice, centered around Boston but occasionally reaching from Exeter, New Hampshire, to Cape Cod. Among his many professional honors were the presidency of the Massachusetts Society of Examining Physicians, the vice-presidency of the Board of Governors of the American College of Surgeons, the presidency of the Association for Surgery of Trauma and a trusteeship of the Massachusetts Memorial Hospitals; he was also wartime consultant on the Medical Advisory Board and chairman of the Committee for Fracture Demonstration for the American Medical Association. His effective work here won several national awards.

One of Morrison's greatest contributions was his service on the State Board of Registration in Medicine. Few doctors realize the importance of this unrewarding, time-consuming and exasperating post, which guards the medical profession from illegitimate practices and which regulates licensure. So intense is the pressure that Board members are subjected to frequent abusive interruptions, and they often receive threats of death, sometimes even requiring State police protection. To this distasteful but essential work, Morrison gave his time persistently, fearlessly and judiciously from 1944 to 1954, being chairman in 1948.

In private life he was universally popular; he was a member of the Harvard Club, the Brae Burn Country Club and the Baalbeck Lodge of Masons. He was married to Alice Blodgett, who survives him with their three sons, Gordon Mackay, Jr., Reid Blodgett and Peter Foster. He will be happily remembered by all who knew him for his professional skill and judgment, his frankness, his buoyance, his loyalty and his unflinching courage.

C.H.B.

CORRESPONDENCE

REGARDING RISK OF SUCCESSIVE SECTIONS

To the Editor: I have read with interest the account of a maternal death adjudged to have been preventable by the Committee on Maternal Welfare in the November 3 issue of the *Journal.* I agree with the Committee that the amount of pontocaine given was "considerably more than is necessary for the satisfactory performance of a cesarean section," but take exception to the opinion that because the patient was undergoing her fourth section, her death might be considered "further evidence that two or three sections *vastly* increase the risk of pregnancy." There is certainly good evidence that a third cesarean section does not materially increase the maternal risk, as indicated by Sullivan and Campbell in an article entitled "One Thousand Cesarean Sections in Modern Era of Obstetrics" (*Obst. & Gynec.* **5**:669-677, 1955), and there is, to my knowledge, no good evidence that a woman undergoing her fourth section is subjected to much more risk than that of the operation itself. Routine replacement of the classic type of cesarean section with its 3 to 4 per cent of uterine rupture by the lower-segment operation with its 0.25 per cent incidence of rupture has materially decreased the risk of post-section childbearing as shown by Coleman in his study, "Classical Cesarean Section Rupture in Pregnancy (*Obst. & Gynec.* **5**:773-780, 1955). In my opinion, each case must be judged individually and a decision to allow further childbearing may safely be made after evaluating the condition of the abdominal cavity and the uterus at the time of section. I would therefore be interested in knowing whether the "vast increase," as quoted above can actually be substantiated.

L. MASTROIANNI, JR., M.D.
Yale University School of Medicine
New Haven, Connecticut

SCIENCE WRITERS PROTEST

To the Editor: Recently, the *Journal* carried some criticism of the manner in which newspapers and other lay mediums handled the announcement of the Salk poliomyelitis vaccine. In general, the tenor of the criticism was that the news was overplayed or exaggerated.

On behalf of the National Association of Science Writers, I should like to call attention to the following quotations which attended the announcement of the 1954 field-trial results:

> From the official news release approved by Dr. Thomas Francis, Jr., of the University of Michigan Poliomyelitis Vaccine Evaluation Center: "The vaccine works. It is safe, effective, and potent . . . There can be no doubt now that children can be inoculated successfully against polio. There can be no doubt that humanity can pull itself up by its own bootstraps and protect its children from the insidious invasions of ultra-microscopic disease."
>
> From Dr. William G. Workman, director, Laboratory of Biologics Control, National Institutes of Health: "It is not too much to say that we have reached today an important milestone in the conquest of poliomyelitis . . . We can go forward with confidence that a major victory has been won in the conquest of poliomyelitis."
>
> From Dr. Alan Gregg, vice president, Rockefeller Foundation: "We can all count ourselves privileged today to

be reverently happy witnesses of a great step forward in the control of infantile paralysis."

From Dr. David Bodian, associate professor of epidemiology, Johns Hopkins University: "The field trial has clearly proved that there is now a way to prevent paralytic poliomyelitis. . ."

Months later, at the annual session in Atlantic City, the House of Delegates of the American Medical Association unanimously voted a resolution citing Dr. Jonas E. Salk for his "monumental contribution to medical science."

Now, then, when men of science shout the news from the rooftops in such superlatives are those who write about science expected to retire to the basement and speak in mere whispers?

JOHN TROAN, *Chairman,*
Committee on Information
National Association of
Science Writers

NOTE: The criticisms that have appeared in the *Journal* regarding the publicizing of the Salk poliomyelitis vaccine have concerned the method of releasing information at the source, not the agencies through which the news was distributed. A search through the *Journal's* pages of the last few months has revealed no mention of the National Association of Science Writers or its members, at least in this relation. *Honi soit qui mal y pense?*—ED.

A SECOND DANIEL

To the Editor: I should like to commend the article by Jones and Finland entitled "Blood Levels from Orally Administered Penicillins G and V" and the accompanying editorial in the November 3 issue of the *Journal.* I am an intern at San Francisco Hospital and during my busy days find myself overwhelmed with a mass of conflicting data, many of which are influenced by the profit motive of drug firms — to the detriment of scientific accuracy.

The article was thoughtfully critical, and supplied the facts for a logical pharmacologic approach to the problem. I should certainly appreciate similar articles.

CARL L. MOLLER, JR., M.D.

San Francisco

RETINOPATHY IN DIABETES

To the Editor: I read with interest the paper by Drs. Klayman and Brandborg entitled "Clinical Application of Cobalt^{60}-Labeled Vitamin B_{12} Urine Test" in the November 10 issue of the *Journal.*

Becker, Lang and Chow, in an article entitled "Vitamin B_{12} Excretion of Diabetic Retinopathy" (*J. Clin. Nutrition* 1: 417-423, 1953), have shown that diabetic patients without retinopathy excreted much less vitamin B_{12} in their urine than nondiabetic patients.

On the other hand the diabetic patient with retinopathy excretes much more vitamin B_{12} than his nondiabetic fellow. If the patient of Klayman and Brandborg later manifests diabetic retinopathy and still excretes an insignificant quantity, I think that they will have shown this case to be a latent pernicious anemia.

STANLEY MIRSKY, M.D.

Chicago

BOOK REVIEW

Casimir Funk: Pioneer in vitamins and hormones. By Benjamin Harrow. 8°, cloth, 209 pp., with 17 illustrations and a frontispiece. New York: Dodd, Mead and Company, 1955. $4.00.

Casimir Funk was one of the great pioneers in vitamin research; it was he who coined the word "vitamin."

Born in Warsaw in 1884, he was educated in Switzerland, did postdoctorate research in Paris and Berlin and worked in laboratories in London, New York, Warsaw, Paris and in New York again, where today (at seventy-two years of age), he continues as an active investigator. During his lifetime he has known such scientific greats as Euler, Fischer, Roux, Metchinikoff, Bertrand, Diels, Abderhalden, Hopkins and Drummond, as assistant, collaborator or friend.

Dr. Funk has lived a restless life as he moved from one laboratory to another in search of a satisfactory environment for his research work. This same restlessness shows in the wide spectrum of his research interests over the years. He has traveled from proteins to carbohydrates to malignant tumors to energy metabolism to DOPA and melanin to beriberi to pellagra to thiamine to cancer and diet to the manufacture of drugs, hormones and vitamin concentrates to bacteriophage to vitamin B_{12} and back to hormones, essentially in that order. The results of his research have been published in over 140 scientific articles and several books. His research work has been competent; some of it has been brilliant.

Professor Harrow comments in this book that Abderhalden worked "extensively rather than intensively." The same thing may be said of Dr. Funk. One is led to wonder what would have happened if his brilliant mind and tireless energy had been devoted to a narrow area of scientific research. For instance, when he found that the crystals he prepared from the "active fraction" of yeast in 1911 did not cure beriberi as he had expected, he might have persisted and finally proved that these were truly crystals of niacin, the antipellagra vitamin. It was not until 1937 that Elvehjem made this discovery. It is clear, from Professor Harrow's account of his life, that Dr. Funk was a strong-willed, scientific prophet who sensed many facts that other investigators later discovered and developed. His has been a useful life, full of activity and interest. He has blazed new trails in important areas of science, and has lived to see these areas exploited.

This interesting book on Dr. Funk is divided into two parts: his life and his work. But his work is his life! In writing about his life Professor Harrow was compelled to draw so much material from his work, that the second part is anticlimactic and often redundant. A clear picture of his personality has not been presented. Nevertheless, this is a good account of the life of a great scientific pioneer.

ROBERT S. HARRIS

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this list must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Amphetamine in Clinical Medicine: Actions and uses. By W. R. Bett, M.R.C.S., L.R.C.P., F.R.S.L.; Leonard H. Howells, B.Sc., M.D., F.R.C.P., physician, United Cardiff Hospitals; and A. D. Macdonald, M.A., M.D., M.Sc., Leech Professor of Materia Medica, Therapeutics and Pharmacology, University of Manchester. 12°, cloth, 78 pp. Edinburgh: E. and S. Livingstone, Limited, 1955. $2.75 (Distributed by Williams and Wilkins, Baltimore.)

Stress Situations. Edited by Samuel Liebman, M.D., medical director, North Shore Health Resort, Winnetka, Illinois, and clinical assistant professor of psychiatry, University of Illinois College of Medicine. 12°, cloth, 144 pp. Philadelphia: J. B. Lippincott Company, 1955. $3.00.

A Synopsis of Medicine. By Sir Henry Letheby Tidy, K.B.E., M.A., M.D., B.Ch. (Oxon.), F.R.C.P. (Lond.), extra physician to Her Majesty the Queen, and consulting physician to St. Thomas's Hospital. Tenth edition. 12°, cloth, 1253 pp. Baltimore: Williams and Wilkins, 1954. $7.50.

Modern Medicine Annual 1955: An annual volume containing the articles that appeared in the twenty-four issues of Modern Medicine during 1954. 12°, cloth, 1636 pp. Minneapolis: Modern Medicine, 1955. $6.00.

Textbook of the Rheumatic Diseases. Edited by W. S. C. Copeman, O.B.E., M.D., F.R.C.P., senior physician, Arthur Stanley Institute for Rheumatic Diseases, Middlesex Hospital, physician in charge of Department of Rheumatic Diseases, West London Hospital, and chairman, Empire Rheumatism Council. Second edition. 8°, cloth, 754 pp., with 464 illustrations. Edinburgh: E. and S. Livingstone, Limited, 1955. $11.00. (Distributed by Williams and Wilkins, Baltimore.)

The Civilian Health and Medical Services. Volume 2. *The Colonies: The medical services of the ministry of pensions; public health in Scotland; and public health in Northern Ireland.* Edited by Sir Arthur Salusbury MacNalty, K.C.B., M.A., M.D., F.R.C.S., F.R.C.P. 8°, cloth, 406 pp. London: Her Majesty's Stationery Office. 1955. 45s. net. (*Medical History of the Second World War.*)

Poliomyelitis. 8°, paper, 408 pp. Geneva: World Health Organization, 1955. Sw.fr.24.- $8.00. (Distributed by the Columbia University Press, New York City.) (No. 26, *World Health Organization Monograph Series.*)

Hematology. By Cyrus C. Sturgis, M.D., professor of internal medicine and chairman, Department of Internal Medicine, University of Michigan Medical School, and director of the Thomas Henry Simpson Memorial Institute for Medical Research, University of Michigan. 4°, cloth, 1222 pp., with 79 illustrations. Springfield, Illinois: Charles C Thomas, 1955. $19.50.

NONCLINICAL NOTES

MASSACHUSETTS MEDICAL BENEVOLENT SOCIETY

At the annual meeting of the Massachusetts Medical Benevolent Society, held at 22 Fenway on December 14, 1955, the following officers were elected for 1955-1956:

President	Paul D. White, M.D.
Vice-President	Leland S. McKittrick, M.D.
Treasurer	Charles C. Lund, M.D.
Secretary	A. William Reggio, M.D.
Trustees for three years	Joseph Garland, M.D.
	Hyman Morrison, M.D.
	Franklin P. Lowry, M.D.

Fellows of the Massachusetts Medical Society are invited to become members of the Benevolent Society by sending a note to that effect, with an appropriate check, to

Dr. Charles C. Lund,
319 Longwood Avenue,
Boston 15, Massachusetts

Annual member	$5.00
Life member	200.00
Benefactor	500.00

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

At the thirty-fifth annual meeting of the Association for Research in Nervous and Mental Disease, the following officers were elected for 1956: president, Dr. Harry C. Solomon; first vice-president, Dr. Stanley Cobb; second vice-president, Dr. Wilder Penfield; secretary-treasurer, Dr. Rollo J. Masselink; and assistant secretary, Dr. Lawrence C. Kolb.

CLINICAL PROFESSOR OF SURGERY

Dr. Charles C. Lund, surgeon-in-chief of the Fifth (Harvard) Surgical Service, Boston City Hospital, in association with Dr. J. Englebert Dunphy, has been appointed clinical professor of surgery at Harvard Medical School.

NOTICES

ANNOUNCEMENTS

Dr. Morton S. Berk announces the removal of his offices to 30 Fenway, Boston 15, for the practice of internal medicine.

Dr. Philip A. Isaacson announces the removal of his office to Four Merriam Parkway, at Upper Common, Fitchburg, Massachusetts, for the general practice of medicine.

ARMED FORCES MEDICAL LIBRARY

The Armed Forces Medical Library announces the publication, in May, of *Bibliography of Medical Reviews.* Copies will be available upon request to the director, Armed Forces Medical Library, Seventh Street and Independence Avenue, Southwest, Washington 25, D.C., in the order of receipt.

THIRD MICROCIRCULATORY CONFERENCE

The Third Microcirculatory Conference will be held at the Hotel Schroeder, Milwaukee, Wisconsin, on Tuesday, April 3. The general topic of the conference will be "Regulation of Blood Flow." A panel symposium entitled "Regulation of Microcirculation in Tissues and Organs" is planned for the afternoon session. Further information may be obtained from Dr. George P. Fulton, Department of Biology, Boston University, 675 Commonwealth Avenue, Boston 15.

SOCIETY MEETINGS AND CONFERENCES

JANUARY 20. Boston City Hospital Hand Service. Page 85, issue of January 12.

JANUARY 20–27. Fifth Panamerican Congress of Gastroenterology. Page 746, issue of October 27.

JANUARY 20 and 27 and FEBRUARY 3. Yale University School of Medicine. Yale-New Haven Medical Center. Page 1092, issue of December 15.

JANUARY 23–26. Consultation Clinics for Crippled Children in Massachusetts. Page 1177, issue of December 29.

JANUARY 25. Boston Committee on Alcoholism. Page 44, issue of January 5.

JANUARY 25, FEBRUARY 29, MARCH 21 and APRIL 25. Massachusetts Heart Association. Page 623, issue of October 6.

JANUARY 25, MARCH 21 and APRIL 26. Phi Delta Epsilon Fraternity Graduate Club Program. Page 118, issue of July 21.

JANUARY 30–FEBRUARY 8, MARCH 19–28 and JUNE 4–13. Army Medical Service Postgraduate Course. Page 84, issue of July 14.

FEBRUARY 6, MARCH 5 and APRIL 2. Fried Lecture Series. Page 535, issue of September 22.

FEBRUARY 13–16. American College of Surgeons. Page 1136, issue of December 22.

FEBRUARY 14. Harvard Medical Society. Page 44, issue of January 5.

FEBRUARY 15, MARCH 28 and APRIL 18. Greater Boston Medical Society. Page 208, issue of August 4.

FEBRUARY 20–22. Atlanta Graduate Medical Assembly. Page 1136, issue of December 22.

MARCH 15–17. American Orthopsychiatric Association. Page 86, issue of January 12.

MARCH 19–22. American Academy of General Practice. Page 1092, issue of December 15.

MARCH 24 and 25. American Psychosomatic Society. Page 260, issue of August 11.

APRIL 3. Third Microcirculatory Conference. Notice above.

APRIL 23–26. International Academy of Proctology. Page 86, issue of January 12.

MAY 2. Postgraduate Medical Institute. Page 487, issue of September 15.

MAY 3–5. American Goiter Association. Page 348, issue of August 25.

MAY 28–JUNE 1. European Symposium on Vitamin B. Page 578, issue of September 29.

JUNE 21–23. Society of Nuclear Medicine. Page 1092, issue of December 15.

JUNE 21–24. American Academy of Dental Medicine. Page 994, issue of December 1.
AUGUST 19–23. American College of Chest Physicians. Page 840, issue of November 10.
SEPTEMBER 10–14. American Dietetic Association. Page 1180, issue of December 29.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, JANUARY 26

THURSDAY, JANUARY 26
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Surgical Grand Rounds. Dr. John Spellman and staff. Saint Elizabeth's Hospital.
*8:45–9:45 a.m. Cardiac Grand Rounds. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*9:00–10:00 a.m. Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*9:00–10:00 a.m. Grand Rounds. Russell Room, House of the Good Samaritan.
*10:00–11:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Guest Speaker of the Bingham Associates. Diagnosis and Management of Scrotal Masses. Dr. Burdick G. Clarke. Cape Cod Hospital, Hyannis, Massachusetts.
*11:00 a.m.–12:00 m. Medical Grand Rounds. Dr. Sylvester McGinn and staff. Saint Elizabeth's Hospital.
*11:00 a.m.–12:00 m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*11:00 a.m.–12:00 m. Pediatric Conference. Mount Auburn Hospital, Cambridge.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*11:15 a.m. Thoracic Conference. The Thoracic Surgical Clinic. Dr. Dwight E. Harken. Main Amphitheater, Peter Bent Brigham Hospital.
*12:00 m. Clinicopathological Conference. Dr. Benjamin Castleman and associates. Pathology Amphitheater, Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Staff Conference. Rehabilitation. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. Orthopedic Clinic. Amphitheater, Peter Bent Brigham Hospital.

FRIDAY, JANUARY 27
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m. Pediatric Grand Rounds. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*12:00 m. Urological Conference. Dr. C. J. E. Kickham, Auditorium, Carney Hospital, Dorchester.
*1:00–3:00 p.m. Combined Medical-Surgical Grand Rounds. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*2:00–3:00 p.m. Pathology Conference. Dr. James Graham. Saint Elizabeth's Hospital.
*4:00–6:00 p.m. X-Ray Conference. Dr. Merrill Sosman. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Morton Street, Jamaica Plain.
*4:30 p.m. Neuroradiologic Conference. X-Ray Conference Room, New England Deaconess Hospital.

SATURDAY, JANUARY 28
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Anesthesia Conference. Dr. Benjamin Etsten. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*8:30–10:00 a.m. Surgical Grand Rounds. Drs. Charles G. Child, III, A. J. A. Campbell and staff. First (Tufts) Surgical Service, New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*10:30 a.m. Teaching Ward Rounds. Ward South 2, Free Hospital for Women.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Hematology Conference (Blood Clinic). Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.

MONDAY, JANUARY 30
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by Entire Surgical Staff and Anesthesia Staff. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:30 p.m. Staff Conference. Child Psychiatry. By appointment. Conference Room (Burnham 7), Massachusetts General Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. X-Ray Conference. Dr. William Carey. Saint Elizabeth's Hospital.
*4:00 p.m. Clinicopathological Conference. Pathology Conference Room, Beth Israel Hospital.
*4:00–5:30 p.m. Anesthesiology Conference. Succinylcholine. Dr. Lipschitz. Surgical Conference Room, Peter Bent Brigham Hospital.
*5:00–6:30 p.m. Anesthesia Group of the Lahey Clinic. Joslin Auditorium, New England Deaconess Hospital.
5:15 p.m. Staff Meeting. Harris Hall, New England Deaconess Hospital.
*7:00–9:00 p.m. Slide Seminar in Pathology. Dr. Edward H. MacMahon. Stearns Auditorium, New England Center Hospital.
*7:00–9:00 p.m. Anesthesia Teaching Conference of Greater Boston. (A) Surgeon-Anesthetist Relations. (B) Job Hunting. Drs. Hand and Audin. Auditorium, Jimmy Fund Building, Children's Medical Center, 35 Binney Street.

TUESDAY, JANUARY 31
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical Grand Rounds. Pathology Conference Room, Carney Hospital, Dorchester.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m.–1:00 p.m. Pediatric Grand Rounds. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*12:15–1:15 p.m. X-Ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
12:30–1:30 p.m. Medical Journal Club. Joslin Clinic. (Cafeteria) New England Deaconess Hospital.
*2:00–3:00 p.m. Hematology Conference. Dr. Mario Stefanini. Saint Elizabeth's Hospital.
*4:00–5:30 p.m. Anesthesia Conference. Dr. Benjamin Etsten. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*5:00 p.m. Surgical Journal Review. Mount Auburn Hospital, Cambridge.
*5:00–6:00 p.m. Service Meeting Followed by Clinical Conference (Medical, Surgical, Obstetrical). Faulkner Hospital.

WEDNESDAY, FEBRUARY 1
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Surgical Grand Rounds. Auditorium, Carney Hospital, Dorchester.
*9:00–10:00 a.m. Surgical Grand Rounds. Massachusetts Memorial Hospitals.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Orthopedic Grand Rounds. Bigelow Amphitheater, White 3A, Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Boston State Hospital Psychiatry Seminar. Reception Building Auditorium, 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Neurology, Neurosurgery and Psychiatry Conference. Drs. Bertram Selverstone, John F. Sullivan and Justin Hope. Stearns Auditorium, New England Center Hospital.
*12:00 m.–1:00 p.m. Roentgen Diagnostic Conference. 5th-floor teaching unit, Beth Israel Hospital.
*12:00 m.–1:00 p.m. Pediatric Clinicopathological Conference. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*12:15 p.m. Vascular Rounds. Drs. Edward A. Edwards and Chilton Crane. D-Main, Peter Bent Brigham Hospital.
*12:30 p.m. Weekly Pathological Meeting. Joslin Auditorium, New England Deaconess Hospital.
*12:30–1:30 p.m. Weekly Staff Review of Autopsies. Dr. William A. Meissner. Joslin Auditorium, New England Deaconess Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*1:00 p.m. Massachusetts General Hospital Hand Clinic, The Clinics of the Massachusetts General Hospital.
*2:00 p.m. Rectal Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Pediatric Conference for Practitioners. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*2:00–4:00 p.m. Postgraduate Medical Institute. Physical and Chemical Methods and Treatment of Psychoses and Psychoneuroses. Drs. Leo Alexander, Robert E. Arnot and Milton Greenblatt. Lemuel Shattuck Hospital, Jamaica Plain.
*2:00–4:00 p.m. Postgraduate Medical Institute. (A) Prenatal Examination. (B) Conduct of Normal Labor and Delivery. Drs. Robert H. Barker and Arthur C. Gorbach, Jr. Lynn and Salem Hospitals, Lynn and Salem.
*4:00–5:00 p.m. Surgical Pathology Conference. Stearns Auditorium, New England Center Hospital.
*4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.
*4:00–6:00 p.m. Overholt Thoracic Conference. Joslin Auditorium, New England Deaconess Hospital.
*6:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*7:30–9:30 p.m. Lahey Clinic Lecture. Joslin Auditorium, New England Deaconess Hospital.

*Open to the medical profession.